International Journal of Anatomy and Physiology ISSN: 2326-7275 Vol. 7 (10), pp. 001-007, October, 2018. Available online at www.internationalscholarsjournals.org © International Scholars Journals

Author(s) retain the copyright of this article

Full Length Research Paper

Assessment of drug interactions in elderly patients of a family health care unit in Aracaju (Brazil): A pilot study

Raquel S. Mendes-Netto[1], Claudia Q. V. Silva[1], Alfredo D. Oliveira Filho[1,2], Chiara E. Rocha[3] and Divaldo P. Lyra-Junior[1]*

[1]Federal University of Sergipe, Av. Marechal Rondon, s/n Jardim Rosa Elze, CEP 49100-000, São Cristóvão, Sergipe, Brazil.

[2]Faculty of Pharmacy, Federal University of Alagoas, Maceio, Brazil.

Accepted 15 May, 2018

This pilot study aimed to assess drug-drug and drug-food interactions in elderly patients of a Family Health Care Unit in Aracaju, Brazil. A descriptive pilot study was performed through an interview questionnaire with 35 elderly patients (28 women) of the Family Health Care Unit. The range of consumed medications was 1 to 7, and the rate was 3.1 medications/person. This pilot study identified that 34 elderly used multiple medication and its related problems such as risk of polypharmacy (5) and drug interaction (34) . The class of drugs most commonly used was related to cardiovascular system, and alimentary tract and metabolism. Prescriptions with 2 to 3, 4 to 5 and 6 to 7 medications showed potential drug-drug interaction (39, 88.8 and 100%, respectively). Some drugs could not be administrated at meal time. These findings highlight the need for additional studies to further evaluate clinical outcomes associated with polypharmacy and potential drug-drug and drug-food interactions.

Key words: Drug-drug interactions, drug-food interactions, elderly patients.

INTRODUCTION

Ageing of the population is the most important demographic change facing many countries around the world, including Brazil (Lima-Costa et al., 2010). As the main drug users in the community, elderly people have become more exposed to the effects of longer therapies and excessive number of drugs during the aging process (Chen et al., 2001).

In Australia, about 80% of the patients over 65-years-old take at least one drug daily (Elliot, 2006). According to literature, the elderly is the largest consumers of prescription and non-prescription medications, as well as dietary supplements, but drug safety information are limited (Moname et al., 1998; Beyth and Shorr, 1999; Qato et al., 2008). Furthermore, the relatively high rates of drug consumption by elderly patients and numerous other factors contribute to the increased prevalence of medication-associated morbidity and mortality affecting this population (Bushardt et al., 2008) . The range of medications used by the elderly is 2 to 5, and considering the over -the-counter drugs, these numbers have a tendency to be higher (Levenson and Saffel, 2007; Vieira, 2007). In Brazil, the elderly constitute 50% of the multiple drug users (Rozenfeld, 2003).

The use of multiple medications, often termed polypharmacy, is recognized as an increasingly serious problem in the healthcare systems (Hajjar et al., 2007; Rozenfeld, 2008). Prevalence of polypharmacy users is an indicator of prescription quality and health care. Besides, it may be understood as an inappropriate medication use, whose consequences include but are not limited to adverse effects, drug-drug interactions, non-compliance with prescribed therapies and unnecessary expenses (Beyth and Shorr, 2002; Rozenfeld, 2003; Rozenfeld, 2008). For elderly patients, polypharmacy complicates drug therapy, increases cost, and is a challenge for healthcare agencies (Rollason and Vogt, 2003; Chumney and Robinson, 2006).

The elderly people are particularly more susceptible to high levels of drugs, which can easily reach higher

*Corresponding author. E-mail: lepfs.ufs@gmail.com, lyra_jr@hotmail.com.

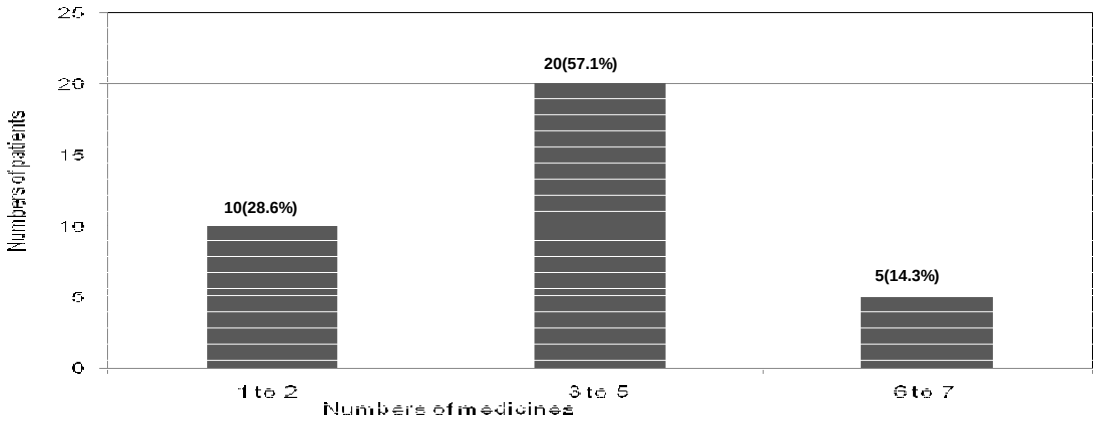

Figure 1. Distribution of number of medication used by elderly patients of a Family Health Care Unit, in Aracaju, Brazil, 2008.

plasma concentrations, once physiologic changes associated with aging include decreased renal elimination, decreased hepatic function, decreased total body water and lean body mass (Pickering, 2004). Beside aging alterations, the use of multiple drugs that affects ingestion, digestion, absorption and, consequently, nutritional status is also common (Pickering, 2004; Heuberger and Caudell, 2011).

The potential risks of multiple drug therapy by elderly are evident, however, so are the benefits to patients when drug therapies are combined to cure, slow the progression or reduce the symptoms of disease (Steinman, 2007; Terrie, 2004). Drug prescription involves the understanding of aging process which can also lead to alterations in the pharmacokinetics of medications for many elderly patients, namely changed distribution, metabolism, and elimination (Turnheim, 2003). Balancing the risks and benefits of multiple drug therapies in older adults, especially to alimentary tract, may be useful in the establishment of rational strategies for the safe use of drugs (Pickering, 2004; Terrie, 2004; Levenson and Saffel, 2007). Therefore, this pilot study aimed to assess drug-drug and drug-food interactions in elderly patients of a Family Health Care Unit in Aracaju, Brazil.

METHODS

A cross-sectional pilot study was conducted at a Family Health Care Unit, in Aracaju City, Brazil. During June 2008, at the health care unit, patients individually interviewed and admitted in consecutive days were included in the study. The sample consisted of 35 individuals, of both genders, 60 years old or more, randomly selected from a list of patients who reported continuous use of at least two prescribed drugs and were enrolled in the government health care programs for hypertension and diabetes. The researchers used a standardized questionnaire which was tested in these individuals to assess its comprehensibility (Appendix A).

Sociodemographic, clinical and pharmacotherapeutics characterization considered in this analysis included patient name, age, gender, drug name, therapeutic indication, pharmaceutical dosage form, time of administration (prior or after meal), and type of beverage during administration. Reported data about drug therapy was checked against the dispensed prescription data.

The *Guanabara Therapeutic Dictionary* (2009/2010) was used to identify prescribed drugs and the *Anatomical Therapeutic Chemical Index* (ATC/DDD Index) developed by the World Health Organization Collaborating Center for Drug Statistics Methodology (2008) was used to classify the drugs into different groups according to the organ or system on which they act (anatomical main group, level 1) and their therapeutic characteristics (therapeutic main group, level 2).

Polypharmacy was defined as the multiple and simultaneously use of five or more drugs in the past seven days (Flahertay et al., 2000). Potentially adverse drug-drug and drug-food interactions were identified by using *Stockley's Drug Interactions*^{TM} (Baxter, 2010) and *Drugdex*^{TM} (2010) databases. Drug-food interactions were classified as adequate or inadequate (Table 4).

Data were recorded and entered into Excel spreadsheets for coding and cleaning and transferred to SPSS v. 17.0 for analyses. The study was approved by the Ethical and Research Committee of the hospital of the Federal University of Sergipe. All participants were informed about the research nature and signed a consent form.

RESULTS

In this pilot study, the sample was constituted by 28 elderly women (80%). Subjects in age range 60 to 84 were 48.57%; from 60 to 69, 40%; from 70 to 79, 79%, and from 80 to 84, 11.42%. All the 35 individuals of the sample related the use of 18 medications. All participants understood the questions made by the researchers.

The reason for multiple drugs use was various diseases or symptoms. 30 subjects (86.7%) indicated hypertension as the main reason; 14 (40%), hypercholesterolemia; and, 13 (37.1%), diabetes. Most of the medications were prescribed by doctors (91.4%), and others were indicated by relative or friend.

The range of consumed medications was 1 to 7, and the rate was 3.1 medications per patient. Of the 35 patients, 5 (14.3%) used 5 or more drugs. Figure 1 shows that 20 elderly (57.1%) consumed simultaneously 3 to 5

Table 1. Medication used, according to the Anatomical Therapeutic Chemical - ATC classification (levels 1 and 2) by elderly assisted by a Family Health Care Unit, in Aracaju, Brazil, 2008.

Medication	ATC Code	n	%
Cardiovascular system	C	53	58
Agents acting on the renin-angiotensin system	C09	21	23
Diuretics	C03	17	18.4
Betablockers	C07	06	6.5
Calcium channel blockers	C08	05	5.4
Antilipemics	C10	04	4.3
Alimentary tract and metabolism	A	18	19.5
Drugs used in diabetes	A10	11	12
Drugs for acid related disorders	A02	04	4.3
Others	A03-A11	03	3.2
Blood and blood forming organs	B	09	10
Antithrombotic agents	B01	07	8
Anti-inflammatory and antirheumatic products	M	02	2.1
	M01	02	2.1
Nervous system	N	05	5.2
Psycholeptics	N05	02	2.1
Antiepileptics	N03	02	2.1
Anti-parkinson drugs	N04	01	1.0
Systemic hormonal preparations, excluding sex hormones and insulins	H	03	3.2
Thyroid therapy	H03	03	3.2
Other medication	N-R-P	04	4.3
Total		92	100.0

Table 2. Relation between medication prescribed and drug-drug interactions by elderly assisted by a Family Health Care Unit, in Aracaju, Brazil, 2008.

Number of prescribed medication	Patient (n)	Prescription with drug-drug-interactions n (%)
2 - 3	23	09 (39.0)
4 - 5	09	08 (88.8)
6 - 7	02	02 (100.0)
Total	34	19 (55.9)

drugs.

Table 1 describes the group of medication used by the elderly according to the ATC index. According to the anatomical classification (level 1), the main consumed medication was related to cardiovascular system (58%) and alimentary tract and metabolism (19.5%). Cardiovascular system acting drugs included those acting on renin-angiotensin system (23%) and diuretics (18.4%). Medications for diabetes (12%) were the most cited as the drugs act on the alimentary tract and metabolism. Other relevant drugs included Antiplatelets (8%) and Beta Blockers (6.5%).

Table 2 shows drug-drug interactions found in the prescription of multiple drugs of 34 elderly. The prescription that had only one medication was considered for the evaluation of drug-meal interaction. It was observed that prescriptions with 2 to 3 (39%), 4 to 5 (88.8%) and 6 to 7 (100%) medications showed potential drug-drug interactions.

The analysis of the potential drug-drug interaction found in the prescriptions is described in Table 3. The medication with potential adverse drug interactions

Table 3. Potential drug-drug interactions with higher incidence according to reports of the elderly assisted by a Family Health Care Unit, in Aracaju, Brazil, 2008.

Association	n (%)
Captopril × Other antihipertensive drugs	09 (25.7)
Diuretics × NSAIDs*	05 (14.3)
Glybenclamide × Captopril	04 (11.4)
ASA** × Captopril	04 (11.4)
Betablockers × Thiazide diuretic	03 (8.6)
Oral hypoglicemiants × Thiazide diuretic	02 (5.7)
Hypoglicemiants × Betablockers	02 (5.7)
Glybenclamide × Metformin	02 (5.7)
Others	06 (17.4)

*Nonsteroidal antiinflammatory;**ASA, acetylsalicylic acid.

Table 4. Drug administration according to meal time of 35 elderly prescriptions assisted by a Family Health Care Unit, in Aracaju, Brazil, 2008.

Drug	Use		Administration	
	N	%	Correct	Incorrect
Captopril	18	51.4	16.7	83.3
Hidrochlorotiazide	17	48.5	58.8	41.2
ASA	07	20.0	85.7	14.3
Propanolol	06	17.1	33.3	66.7
Glybenclamide	06	17.1	83.3	16.7
Metformine	04	11.4	50.0	50.0
Methyldope	04	11.4	100.0	-
Nifedipine	04	11.4	-	100.0

administered in the same time or interval that was frequently found includes Captopril × Other hypotensive agents (25.7%, n = 9), diuretics × non-steroidal anti-inflammatory drugs (NSAIDS) (14.3%, n = 5) and acetylsalicylic acid (ASA) × captopril (11.4%, n = 4). Although other drug interactions were less frequently observed, these interactions also represent a risk of health related problem in elderly.

The administration of medication associated with and/or in proximity to meals was analyzed according to the literature (Table 4). Nifedipin, captopril and propranolol administration had the highest percentage of inadequate use among elderly. Conversely, methyldopa, ASA, glybenclamide, hidrochlorotiazide had the highest percentage of adequate use associated or not with meals.

DISCUSSION

The present study corroborates researches carried out in Brazil which have demonstrated that medication consumption is consistently associated with female gender and elder population (Romano-Lieber et al., 2002; Lyra et al., 2007; Rozenfeld et al., 2008). According to literature, the relationship between age and consumption of multiple drugs can be explained by increased health problems in old age, especially long- term and more severe diseases which treatment and symptom relief demands drug therapy intervention (Rollason and Vogt., 2003; Chumney and Robinson, 2006; Craig, 2006).

Concerning the gender, the female predominance was also reported in population studies of elderly (Chen et al., 2001; Rollason and Vogt, 2003; Elliot, 2006; Rozenfeld et al., 2008). Many factors underlies the higher longevity of women such as cardiovascular protection by female hormones, decreased aggressive behavior, lower risk for accidents at work, higher attention to symptoms, higher use of health care, lower consumption of cigarette and alcohol, and others. However, it must be considered that male patients in the same age group may also be susceptible to polypharmacy but did not attend the study setting.

The rate found of used drugs per elderly (3.1) is

according to other studies which range 2.1 to 3.6 drugs per person (Rollason and Vogt, 2003; Lyra et al., 2007; Rozenfeld et al., 2008). The use of multiple drug by people over the age of 60 have also been reported (Beyth and Shorr, 1999; Rollason and Vogt, 2003; Rozenfeld et al., 2008), reinforcing the concern with the drug administration in this subgroup of Brazilian population.

The predominance of the drugs from cardiovascular (58%) and alimentary tract and metabolism (19.5%) groups has been described in literature (Chen et al., 2001; Coelho et al., 2004; Lyra et al., 2007; Heuberger and Caudell, 2011). The presence of 6 cardiovascular drugs, and especially four drugs for arterial hypertension, reflects the morbidity and mortality found in Brazil and also the fact that hypertension was the most cited chronic disease by the elderly participants (Coelho et al., 2004; Loyola et al., 2006; Lyra et al., 2007).

The most used drugs were Angiotensin-Converting Enzyme Inhibitor (ACEI), followed by Diuretics, Beta-Blockers, and Calcium Channel Blockers. Fick et al. (2003) point out the increasing prescription of ACEI and Calcium Channel Blockers, instead of Diuretics and Beta Blockers. Even though in the present study it was not observed, it is important to result that nervous system acting drugs are usually prescribed for the elderly for the treatment of insomnia, anxiety, and confusion (Coelho et al., 2004). One possible reason is that the health care unit does not provide the distribution of those agents.

As described by other authors (Lyra et al., 2007; Rozenfeld et al., 2008), the majority was prescribed medications (83.8%) . It is reasonable that the society pays more attention to the elderly care. Besides, the participants belonged to a group education and had relative easy access to health care services (Vasconcelos et al., 2005; Rozenfeld et al., 2008). According to Rozenfeld (2003), some factors contribute to discouraging the acquisition of unnecessary products between the elderly, including: Low retirement income and pensions, and lack of adherence to chronic disease treatment (complexity, memory loss, and others).

The results obtained confirm relationship between the number of drugs and the drug-drug interactions. According to the analysis, the higher the number of medications, the higher the exposition to one or more adverse drug interaction (Rozenfeld, 2003; Sehn et al., 2003; Qato et al., 2008) (Table 2). In a study with 40 patients, Sehn et al. (2003) found potential drug-drug interactions in 25% of the prescriptions containing up to 5 drugs, 63.6% containing 6 to 10, and 100% containing more than 10. Therefore, polypharmacy has an important role in the frequency of drug interaction. The medications involved are known and routinely used, and the effects can be predictable (Rollason and Vogt, 2003; Bushardt et al., 2008).

The literature (Romano-Lieber et al., 2002; Terrie, 2004; Bushardt et al., 2008) affirms that measures to avoid or minor such effects include adjustment of therapeutic dose, simplification of time of administration; consideration of each details of the elder patient such as the habit of using medications, life style, social and mental levels, degree of physical dependence, and others; clear description of all the instructions about the importance of the correct medicament use, period of treatment and possible side effects to both the elderly and people involved in the elder care; attention to the therapeutic outcomes and complicating pathologies; and, have in mind that both effective and toxic dose reduce with age.

In routine, it is technically difficult to have a complete control over all the prescribed drugs and their possible interactions. Nevertheless, the health care professionals, including pharmacists, should be concerned about the medication that are most commonly used and have high potential of drug interaction (Romano-Lieber et al., 2002; Terrie, 2004; Chumney, Robinson, 2006; Bushardt et al, 2008). The outcomes from an interaction can increase the therapeutic effect, reduce the effectivity, cause different levels of adverse reactions, or even have no effect on the desired action of the drug (Rollason and Vogt, 2003; Elliot, 2006). Thus, drug interaction can be beneficial, adverse or have a little clinical significance.

Common drug interactions were described in Table 3. Sehn et al. (2003) suggest an analysis of the risks to the health patient according to the severity of the drug-drug interaction consequences. According to this, three interactions were classified as severe. Theses interactions that might be life-threating and cause permanent injury are as follows: diuretic × NSAIDS (risk of renal insufficiency), and glybenclamide × captopril and glybenclamide × metformin (risk of hypoglycemia, both).

Other four identified interactions that may represent a moderate risk, like hyperglycemia and increase of arterial pressure, are as follows: ASA × captopril; beta blockers × thiazide diuretics; oral antidiabetics × thiazide diuretics; and, antidiabetics × beta blockers). captopril × other hypotensive agents was identified as a mild interaction and can result in undesirable hypotension.

The extent of drug absorption is influenced by the presence and type of food in alimentary tract (Pickering, 2003; Santos and Boulata, 2005). This association may be necessary if drug of choice causes gastric irritation or if concurrent presence of food increases drug absorption. Association between medication intake routine and regular meals can also lead to better medication adherence outcomes (Moura and Reyes, 2002). In a study with 60 inpatients (Lopes et al., 2010) 19.5% of drug-food interaction in 82 medical prescriptions was identified.

It is relevant to highlight that the oral route is the main drug administration form; the drug-food interaction occurs mainly in the alimentary tract. Those interactions includes alteration of drug-nutrient complex formation and absorption of both drug and nutrient, and also effects on

drug distribution, metabolism, excretion and local of action (Genser, 2008; Pickering, 2003; Santos and Boulata, 2005). Physiological effects should be also considered such as modifications of appetite, digestion, gastric emptiness and drug-induced renal failure (Moura and Reyes, 2002; Santos and Boulata, 2005).

Table 4 shows the utilization patterns of most cited medicaments. Nifedipine should be administrated without food to reduce the incidence of side effects (Moura and Reyes, 2002), and simultaneous drug and food ingestion retard but do not reduce absorption. Captopril absorption can be reduced up to 50%; thus, it should be administrated 2 to 3 h after or 1 h before the meals (Moura and Reyes, 2002). In contrast, the bio- availability of propanolol is increased, when ingested with a protein-rich meal (Pickering, 2004). For this reason, propranolol should be also administrated 2 to 3 h after or 1 h before the meals (Moura and Reyes, 2002). This interaction can lead to a toxic effect of the drug and promote glucogenolysis and hypoglycemia (Parameshappa et al., 2010).

CONCLUSION

The assessment of drug therapy used by elderly patients attended by Family Health Care Unit in Aracaju, Brazil showed polypharmacy and, in consequence, drug-drug and drug-food interactions in this population. General principles of clinical care and prevention of undesirable effects of polypharmacy, and drug-drug and drug-food interactions involves the correct counseling about time of administration of different medicaments, with or without food and/or liquid.

Understanding the possible interactions and adverse outcomes of polypharmacy in respect to mechanisms, careful observation and monitoring of the elderly patient can help multiprofessional health care teams to reduce the risk and the severity of interactions, optimizing the effectiveness and minimizing the toxicity of drug and nutritional therapeutics.

The findings obtained in the present study point out the relevance of conducting more studies to deeply explore this event, drug therapy and nutritional follow-up, considering the need of adjustment of dosage and time of administration, nutritional supplementation, and alternative treatment viability.

REFERENCES

ATC/DDD Index (2008). Who Collaborating Centre for Drug Statistics Methodology. Available at:<http://www.whocc.no/atcddd>. Acessed on june 10, 2008.

Baxter K (2010). In: Stockley's Drug Interactions, 9th Edn. Pharmaceutical Press, p. 1472.

Fick DM, Cooper JW, Wade WE, Waller JL, Maclean JR Beers MH (2003) Updating the Beers Criteria for potentially inappropriate medication use in older adults. Arch. Intern. Med., 163(22): 2716–2724.

Beyth RJ, Shorr RI (2002). Principles of drug therapy in older patients: rational drug prescribing. Clin. Geriatr. Med., 18(3): 577-592.

Beyth RJ, Shorr RI (1999). Epidemiology of adverse drug reactions in the elderly by drug class. Drugs Aging., 14(3): 231-239.

Bushardt RL, Massey EB, Simpson TW, Ariail JC, Simpson KN (2008). Clin. Interv. Aging., 3(2): 383-389.

Chen YF, Dewey ME, Avery AJ (2001). The Analysis Group of the MRCCFA Study. Self-reported medication use for older people in England Wales. J. Clin. Pharm. Therap., 26(2): 129-140.

Chumney EC, Robinson LC (2006). The effects of pharmacist interventions on patients with polypharmacy. Pharm. Practice, 4(3): 103-109.

Coelho Filho MJ, Marcopito FL, Castelo A (2004). Medication use patterns among elderly people in urban area in Northeastern Brazil. Rev. Saude Publica, 38(4): 557-64.

Drugdex® System. Greenwood Village (2010). Thomson Micromedex® Healthcare Series 20: Interactions, 2010. Available at: <http://periodicoscapesgovbr>. Acessed on Feb 15, 2010.

Elliott RA (2006). Problems with medication use in the elderly: an Australian perspective. J. Pharm. Pract. Res., 36(1): 58-66.

Flaherty JH, Perry HM, Lynchard GS, Morley JE (2000). Polypharmacy and hospitalization among older home care patients. J. Gerontol., 55(10): M554-559.

Genser D (2008). Food and drug interaction: consequences for the nutrition/health Status. Ann. Nutr. Metab., 52(suppl 1): 29–32

Hajjar ER, Cafiero AC, Hanlon JT (2007). Polypharmacy in elderly patients**.** Am. J. Geriatr. Pharmacother., 5(4): 345-51.

Heuberger, RA, Caudell, K (2011). Polypharmacy and nutritional status in older adults: a cross-sectional study. Drugs Aging, 28(4): 315-323

Korolkovas A, França FFAC (2009). Dicionário terapêutico Guanabara: 2007/2008, 14th Edn. Guanabara, p. 628.

Levenson SA, Saffel DA (2007). The consultant pharmacist and the physician in the nursing home: roles, relationships, and a recipe for success. Consult. Pharm., 22(1): 71-82.

Lima-Costa MF, Firmo JOA, Uchoa E (2010). Cohort profile: The Bambuí (Brazil) cohort study of ageing. Int. J. Epidemiol., [Epub ahead of print August 30, 2010].

Lopes EM, Carvalho RBN, Freitas RM (2010). Analysis of possible food/nutrient and drug interactions in hospitalized patients. Einstein, (3 Pt 1): 298-302.

Loyola Filho AI, Uchoa E, Lima-Costa MFF (2006). A population-based study on use of medication by the elderly in greater metropolitan Belo Horizonte, Minas Gerais, Brazil. Cad. Saude Publica, 22(12): 2657–2667.

Lyra DP, Kheir N, Abriata JP, Rocha CE, Santos CB, Pelá IR (2007). Impact of Pharmaceutical Care interventions in the identification and resolution of drug-related problems and on quality of life in a group of elderly outpatients in Ribeirão Preto (SP), Brazil. Ther. Clin. Risk Manag., 3(6): 989-998.

Moname M, Mathias DM, Nagle BA, Kelly MA (1998). Improving prescribing patterns for the elderly through an online drug utilization review intervention: a system linking the physician, pharmacist, and computer. JAMA**.,** 280(14): 1249-52.

Moura MRL, Reyes FGR (2002). Drug-nutrient interaction: a review. Rev. Nutr., 15(2): 223-238.

Parameshappa B, Rao NV, Gouda TS, Sen S, Chakraborty R, Basha MA, Reddy AS, Kumar SMS (2010) A study on drug-drug interaction between anti-hypertensive drug (propranolol) and anti-diabetic drug (glipizide). Ann. Biol. Res., 1 (3): 35-40.

Pickering G (2004). Frail elderly, nutritional status and drugs. Arch. Gerontol. Geriatr., 38: 174-180.

Qato DM, Alexander GC, Conti RM, Johnson M, Schumm P, Lindau ST (2008). Use of prescription and over-the-counter medications and dietary supplements among older adults in the United States. JAMA., 300(24): 2867-2878.

Rollason V, Vogt N (2003). Reduction of polypharmacy in the elderly a systematic review of the role of the pharmacist. Drugs Aging, 20(11): 817-832.

Romano-Lieber NS, Teixeira JJV, Farhat FCLG, Ribeiro E, Crozatti MTL, Oliveira GSA (2002). A literature review on pharmacists' interventions in the use of medication by elderly patients. Cad. Saude Publica, 18(6): 1499-1507.

Rozenfeld S (2003). Prevalence, associated factors, and misuse of medication in the elderly: a review. Cad. Saude Publica, 19(3): 717-724.

Rozenfeld S, Fonseca MJM, Acurcio FA (2008). Drug utilization and polypharmacy among the elderly: a survey in Rio de Janeiro City, Brazil. Rev. Panam. Salud Publica, 23(1): 34–43.

Santos C, Boullata J (2005). An approach to evaluating drug-nutrient interactions. Pharmacotherapy, 25(12): 1789–1800

Sehn R, Camargo AL, Heineck I, Ferreira MBC (2003). Interações medicamentosas potenciais em prescrições de pacientes hospitalizados. Infarma, 15(9-10): 77-81.

Steinman MA (2007). Polypharmacy and the balance of medication benefits and risks. Am. J. Geriatr. Pharmacother., 5(4): 314-316.

Terrie YC (2004). Understanding and managing polypharmacy in the elderly. Pharm. Times, 12(2): 84-87.

Turnheim K (2003). When drug therapy gets old: pharmacokinetics and pharmacodynamics in the elderly. Exp. Gerontol., 38: 843–853.

Vasconcelos FF, Victor JF, Moreira TMM, Araújo TL (2005). Use of medication for seniors of a basic unit of health of the family of Fortaleza-CE. Acta. Paul. Enferm., 18(2): 178-183.

Vieira FS (2007). How pharmacists can contribute to health promotion. Cienc. Saude Coletiva, 12(1): 213-220.