ABSTRACT

Background

Elderly people have a high risk of potentially inappropriate medications (PIMs) and drug-related problems (DRPs) due to polypharmacy, physical and mental limitations, pharmacokinetic, and pharmacodynamics changes.

Purpose

To determine the role of geriatric pharmacists in reducing drug-related problems and potentially inappropriate medication.

Methods

The observational study was conducted from October 2014 to October 2017 to show the prevalence of DRPs, and PIMs. A total of 375 geriatric cardiology patients (aged ≥ 65) were recruited from Geriatrics Cardiac Clinic in Saudi Arabia. AGS Beers Criteria 2012 and STOPP/START Criteria were used to view the impact of services directed by clinical pharmacists in decreasing DRPs and PIMs including medication review, intervention, and education to junior physicians during multidisciplinary rounds (MDRs) and by sending e-mail alerts.

Results

DRPs were found in 29.6% of patients and PIMs were found in 19% of patients. After medication review, 25% required interventions and the majority (89%) of interventions were accepted by the managing team. DRPs were found in 14.9% of patients and PIMs were found in 9.6% of the patients. DRPs and PIMs were reduced almost by 50% by reviewing the files and educating the involved physicians.

Conclusion

This prospective study confirms a high prevalence of DRPs and PIMs in Saudi elderly cardiac patients.

Key words: cardiac, drug-related problems, geriatrics, potentially inappropriate medication

INTRODUCTION

It is a fact that the number of elderly people is growing worldwide. In 2050, the elderly population worldwide is expected to be increased and reach 2 billion. The percentage of Saudi Arabian people over 64 years of age was 3.5% of the total Saudi population in 2014 and is projected to increase 3 times by the year of 2030. This group is at risk of multiple medical problems, such as potentially inappropriate medications (PIMs) and drug-related problems (DRPs). PIMs in geriatrics are defined as a medication in which the risk of side effects outweighs its benefit, particularly if there is a safer alternative available for this condition. In elderly people, PIMs have a significant impact on patient safety and quality of life. DRPs are defined by Hepler and Strand as “an event or situation involving drug therapy that actually and potentially interferes with optimum outcome for a specific patient.” In elderly people, DRPs involves numerous risks. The high prevalence of PIMs in the elderly seems to be a global problem in all managed care settings, including ambulatory care setting.

The distinct changes in endogenous neurotransmitter concentrations within the nervous system makes elderly people with dementia more prone to drug-related problems. The concerns related to consequences of using inappropriate drugs have been reported, frequently. Moreover, intake of inappropriate drugs increases the risk of severe adverse event...
resulting in hospitalization. It has been shown that hospitalization due to drug-related causes is most commonly observed among elderly people suffering from dementia.\(^{(5)}\) Previous study has shown that involvement of pharmacists within the health-care team was not beneficial for reducing drug-related hospital admission.\(^{(6)}\) However, it was shown that there is a significant impact of interventions on post hoc and subgroups during the first 30 days following intervention among the individuals without any cardiac complication. Therefore, the present study has mainly focused on analyzing the secondary outcomes and major reasons for drug-related readmissions among the individuals with cardiac complications.

This study aims to investigate both PIMs and DRPs in Saudi Arabian elderly people and identify risk factors associated with PIMs and DRPs (Figure 1). The risk factors in the study are polypharmacy and following cardiac clinic in more than one hospital, as well as age, gender, over-the-counter medications, and literacy levels.\(^{(5,7,8,9)}\) Furthermore, this study has explored the potential role of geriatric pharmacists in medication management and in reducing PIMs and DRPs. Lastly, this study has observed the rate of prescribing high-alert medications and medications with a narrow therapeutic index, as well as herbals and over-the-counter (OTC) medications among Saudi Arabian elderly patients. Moreover, quality improvement project, pharmacy-based trial screening, DRPs and PIMs were performed to investigate whether a clinical pharmacist-led intervention reduces the number of DRPs and PIMs in geriatrics patients aged ≥65 years attending cardiology clinic.

**METHODS**

**Research Design**

This quality improvement project was carried out over three years and conducted in a cardiology ambulatory care setting at a major hospital in Riyadh, Saudi Arabia. A Geriatric Pharmacist interviewed 750 patients, who attended the cardiac clinic and who were randomly chosen for medication review (every third geriatric patient attended the clinic) in two stages.

**Procedure**

In the first stage, 375 geriatric cardiac patients and their families were interviewed and the files were reviewed from October 2014 to April 2016. Baseline demographic data were collected: age, sex, marital status (married or not), and follow-up in more than one hospital were documented. PIMs were assessed using 2012 AGS Beers Criteria and 2008 revised STOPP/START Criteria (Figure 1). DRPs were broken down in this study into seven domains where PIMs were considered as a domain from DRPs (Figure 2). PIMs were divided into overtreatment (STOPP criteria), and under treatment (START criteria). Potentially inappropriate medication was used in older adults (Beers Criteria) because safer alternative is unavailable, whereas potentially inappropriate medication was used in older adults due to drug disease or drug-syndrome interactions (Beers Criteria) that may exacerbate the disease or syndrome.

Others DRPs were: subtherapeutic dosage (indicated medication, but dose too small), overdosage (indicated medication, but dose too large), adverse drug reactions (side effects of medications), drug interactions (presence of drug or drug food interactions), drug duplication (more than one medications from the same class of drugs such as two angiotensin-converting enzyme from two different caregivers), and failure to receive medication (a medical condition resulting from failure to prescribe a medication because medication was out of stock or any other reason when indicated).

**Interventions**

All high-alert medications on the list published by the Institute for Safe Medication Practice (ISMP) were recorded. This list includes medications that can cause harm if used inappropriately. Use of herbal medications and medications with low therapeutic index were recorded. Low therapeutic index is defined as a medication with a narrow range between the drug’s risks and its benefits. The percentage of interventions recommended after review was also recorded. Interventions were defined as a recommended change with the Primary Physicians/Managing team. Explanations were given for these recommendations, and the percentage of the recommendations accepted or rejected was also recorded. All rejected recommendations were documented in pharmacist notes, along with the summary of discussion with the managing team. Recommendations given to patients without involving the managing team were not defined as interventions. This study has implemented teaching and meetings with other members during bi-weekly multidisciplinary round (MDR),
which raised awareness of DRPs and PIMs among cardiac physicians, as well as involving the pharmacists in medication chart reviewing. This study continued with bi-weekly MDRs and meetings from October 2014 to April 2016 (Figure 2).

Stage two started October 2016 to October 2017 and 375 patients were randomly chosen. Medication reviews were performed to evaluate the prevalence of DRPs and PIMs and to assess the rate of improvement. The individuals using more than three medications referred to as polypharmacy with multimorbidity were recruited. For instance, polypharmacy is likely to be associated with adverse drug reactions, long hospital stays, mortality, and readmissions. Informed consent of all participating patients was obtained by signing written agreement. The research complied with the ethical rules for human experimentation that are stated in the Declaration of Helsinki (https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/). The study was approved by the institutional review board at the hospital where this study was conducted. The data were analyzed using SPSS (Version 21).

Statistical Analysis

A database was established and analyzed by SPSS (Version 21). Descriptive statistics are shown as means with SD for continuous variables and as frequencies for categorical variables. Tests for differences between the two groups were performed by Pearson’s chi-squared tests for categorical variables, and by independent samples t-test for continuous variables. The 95% confidence interval (CI) was performed to assess the influence of polypharmacy, gender, age and literacy risk factors in the two groups. The results were assessed and measured at 5% level of significance.

RESULTS

Stage One

A total of 375 elderly patients (male 51%; female 49%) were included in the study. Participants’ characteristics are shown in Table 1. Rate of illiteracy was 51%, while polypharmacy was seen in 82% patients. Use of herbal medications was documented in 8% of patients, while most patients were not aware of the common herbal remedies contribute to DRPs and PIMs.

The details of DRPs are shown in Table 2, which shows detection of DRPs among 111 (30%) geriatric patients from October 2014 to April 2016. PIMs represent majority of DRPs where inappropriate medication was documented in 70 (19%) patients. Among the 70 patients identified with PIMs, 40 (47%) documented STOPP/START Criteria and 30 (43%) were documented by using Beers Criteria. The most common PIMs according to Beers Criteria were: taking long-acting oral hypoglycemic drugs, mainly Glibenclamide; and prolonged use of antihistamines and antipsychotic medications without proper indication. The most common PIM documented using STOPP/START Criteria was proton pump inhibitors (PPI), either overuse or underuse. The overuse was

![Figure 2. Classification of drug-related problems](image-url)
simply using PPI beyond eight weeks without clear indication. Underuse of PPI represented by patients’ undergoing a dual anti-thrombotic therapy, like aspirin and clopidogrel, without a prophylactic dose of PPI.

There was a significant positive correlation between polypharmacy and the prevalence of DRPs and PIMs, ($r=0.49$; $p<0.002$). There was a significant positive correlation between patients who attended more than one cardiac center and the prevalence of PIMS ($r=0.343$; $p<0.03$). There were 90 (25%) patients for whom an intervention was recommended. In this context, 80... (89%) patients recommended interventions were accepted by the managing team (Table 3). The findings have shown that psychotropic medications were main recommendations that were not supported. Furthermore, the main reason of rejection of medication was that it was prescribed from other centers, or because of fear of consequences of discontinuation. The use of OTC and herbal medications were not related to level of education. High-alert medication was documented in 75 patients (21%). The most common were insulin, oral hypoglycemic medications, and oral anticoagulant. Medications with low therapeutic index were recorded in 29 (8%) patients.

**Stage Two**

A total of 375 elderly patients (72 ± 6.2 years old; 52%) were included in stage two study. DRPs were detected in 56 (15%) geriatric patients characteristics shown in table 3. The prevalence of inappropriate medication was documented in 27 (7%) patients making 48% of DRPs. Among the 27 patients identified with PIMs, 13 (48%) patients documented STOPP/START Criteria and 14 (52%) patients documented the use of Beers Criteria (Table 4).

**DISCUSSION**

Although, PIM is common, few studies address prospective interventions to reduce PIMs. This medication review resulted in interventions in a quarter of patients. The acceptance rate of interventions was high. In one study, review of renal cleared medications in an aged facility by a certified pharmacist resulted in acceptance of 84% of recommendations by general practitioners. In another study, home medication review by a community pharmacist resulted in 28% reduction of PIMs in community dwelling elders. Methods used to reduce PIMs include inpatient geriatric consultation team. This has shown efficacy in a randomized trial on a group of inpatient elders using the STOPP criteria. Education of patients and or providers is another intervention shown to reduce PIMs. Finally, computerized algorithms and aids can reduce PIMs. There are no prospective studies comparing various interventions to reduce PIMs. The most appropriate, reliable, and cost-effective method is yet to be determined.

A large study has shown that PIM is associated with increased mortality. However there is lack of evidence on impact of reducing PIMs on mortality. Arguments exist about the benefits reducing PIMs on other important outcomes. This evidence has been reported in different populations and settings, exploring at different outcomes. Several common outcomes addressed by these studies include adverse events leading to Emergency Department (ED) visits, hospital admissions (HA), and potential for cognitive impairments, falls, and reduced quality of life. In several studies, reducing PIMs decreased ED visits and HA. In a palliative care setting, reducing PIMs did not result in improvements in quality of life.

Although PIMs is the most common DRP, other medication-related problems exist. An important finding was that almost one-third of the elders were on high-alert medications and medication with a low therapeutic index. Moreover, polypharmacy was prevalent as the use of herbal medication is rising. The elders perceive these as natural products and safe. Renal, hepatic, dermatological, and cardiovascular adverse effects have been reported with these herbs. There lacks knowledge about the potential interactions with prescription medication. These factors compete with PIMs in reference to adverse outcomes related to medications and the complexity of evaluating many important patient outcomes.

The study concurs with studies that report that the use of Beers and STOPP/START criteria is complimentary in evaluating and detecting PIMs. The most common PIMs associated with Beers oral hypoglycemic agents, antihistamines and antipsychotic, and STOPP/START criteria identified PPI.

| Characteristic | Number | Percentage |
|---------------|--------|------------|
| Age           | 72 ± 6.2 | 100% |
| Male          | 195     | 52% |
| Female        | 180     | 48% |
| Polypharmacy  | 285     | 76% |
| Rate of literacy | 240  | 64% |
| High-alert medications | 70   | 18.7% |
| Medication with low therapeutic index | 34 | 9% |

| TABLE 3. Baseline characteristic of stage two |
|---------------------------------------------|
| Characteristic | Number | Percentage |
|----------------|--------|------------|
| Age            | 72 ± 6.2 | 100% |
| Male           | 195     | 52% |
| Female         | 180     | 48% |
| Polypharmacy   | 285     | 76% |
| Rate of literacy | 240  | 64% |
| High-alert medications | 70   | 18.7% |
| Medication with low therapeutic index | 34 | 9% |

| TABLE 4. Details of drug-related problems in stage two |
|------------------------------------------------------|
| Characteristic | Number | Percentage |
|----------------|--------|------------|
| Medication-related problems | 56 | 14.9% |
| Potentially inappropriate medications | 36 | 9.6% |
| Drug interaction | 7 | 1.9% |
| Adverse drug events | 4 | 1% |
| Drug duplications | 3 | 0.8% |
| Overdose | 2 | 0.53% |
| Underdose | 0 | 0 |
| Failure to receive medication | 4 | 1% |
as the most common (PIMs Saudi Arabia). The list of most common PIMs seems to be related to local practice. (20)

CONCLUSION

The present study has confirmed a high prevalence DRPs and PIMs in Saudi elderly cardiac patients. Medication review by clinical pharmacists through MDRs is a simple, reliable method to reduce DRPs and PIMs. It is important to optimize patient safety and minimize toxicity of medications in this increasing population of senior patients. Overall, this study has demonstrated that pharmacist-led interventions improve the prescribing appropriateness among the community-dwelling older adults with cardiac problems. The pharmacist working in a multidisciplinary primary care team requires further investigation to optimize prescribing in this group of patients.

There is a significant impact of medication review and feedback during ward rounds on the readmission rates of elderly people. The study has suggested that special attention, along with improved cooperative activity among the health-care providers, should be offered to individuals living at home who are suffering from chronic disease like cardiac complications. The study results are limited as the study has been conducted in a real-life setting; however, the results have depicted significant impact, although the patients were recruited from a selected ward. The sample size used in this study was not calculated using power analysis; rather it was done through convenient sampling.

It would be interesting to apply this quality improvement project to geriatrics as a mean of reducing the effects of ADEs. The high acceptance of interventions with appropriate explanations is worthy to be considered for a larger group. Prospective studies are needed to define the most appropriate and cost-effective measure to reduce DRPs. Future studies should identify the impact of reducing DRPs on predefined patient-related outcomes.

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CONFLICT OF INTEREST DISCLOSURES

The authors declare that no conflicts of interest exist.

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