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Risk Factors for Developing Drug Related Problems in Patients with Cardiovascular Diseases

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ABSTRACT

Medicines have been playing important role in the cure, palliation as well as inhibition of diseases, but they also expose patients to Drug related problems (DRPs). Drug related problems constituted a major safety issue among patients with cardiovascular diseases (CVDs). These not only cause patient harm and increase health care costs but also lead to negative clinical outcomes[1]. Prescriptions containing multiple medications not only increase complexity of treatment regimen but also make the patient poorly adherent to those prescribed medications [2]. According to a study, the frequency of Drug Related Problems (DRPs) has been reported to be as high as 69% and 78% respectively in patients with cardiovascular diseases[1,3]. The aim of the study is to assess the risk factors for developing drug related problems in patients with cardiovascular diseases. Analysis of original research articles has been done to assess the risk factors associated with DRPs in patients with cardiovascular diseases. The common DRPs were found to be inappropriate selection of drugs, improper dosages, adverse drug reactions and drug interactions[4,5]. The risk factors found to be associated with DRPs in patients with CVDs were old age, female gender, poly pharmacy, and potential drug-drug interactions, multiple diseases, lack of therapeutic monitoring, need of additional drug therapy, associated co-morbidities, length of hospital stay and drugs like anti coagulants, diuretics, beta blockers and lipid lowering agents etc[6,7]. Hence there is a need for clinical pharmacist's interventions to identify, monitor and prevent the risk of developing Drug Related Problems and contribute to improve the clinical outcome in patients with cardiovascular diseases.

Key words: Drug related problems, cardiovascular diseases, risk factors and clinical outcome.

INTRODUCTION

Cardiovascular diseases (CVDs) are a group of disorders of the heart and blood vessels and they include coronary artery disease, cerebro-vascular disease, peripheral arterial disease, rheumatic heart disease, congenital heart disease, deep vein thrombosis and pulmonary embolism and stroke. CVD is a major cause of morbidity and mortality worldwide with the life time risk exceeding 64% [8].

According to World Health Organization (WHO), CVDs are the number one cause of death globally, representing 31% of all global deaths [9].

Pharmacotherapy plays an essential role in reducing morbidity and mortality related to cardiovascular diseases. However, these advantages are limited by drug related problems that can impact on a patient's quality of life, prolong hospital stays and increase the overall burden of healthcare expenditures [10].

Drug-related problem (DRP) is defined as 'an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes'[5]. DRPs often constitute a safety issue among hospitalized patients leading to patient harm and increased healthcare costs. The term DRP includes medication errors

(MEs), adverse drug events (ADEs) and adverse drug reactions (ADRs). A medication error is 'any preventable event that may cause or lead to inappropriate medication usage while medication is still in the control of the healthcare professional, patient or consumer [10]. An adverse drug event is defined as 'an injury –whether or not casually related to use of a drug'. An ADR can be defined as 'any response to a drug which is noxious and unintended, and which occurs at doses normally used in humans for prophylaxis, diagnosis or therapy of diseases, or for the modification of physiological functions' [11].

Drug related problems or drug therapy problems (DTPs) can occur at all steps of the treatment process, mainly during prescribing, transcribing, dispensing and use of medication by patient[12]. These problems not only influence the treatment outcomes of the patient but also affect the ability to achieve the desired therapeutic goals.

Recently, the use of polypharmacy has increased in patients with cardiovascular diseases, mainly because of the higher number of associated comorbidities in this group of patients [1,3,13]. Specifically, heart failure involves the management of multiple medical conditions, requiring a significant increase in the mean number of drugs from admission to discharge [1].

The early identification and modification of risk factors has been shown to reduce mortality and morbidity in people with diagnosed or undiagnosed cardiovascular disease [5].

OBJECTIVE:

Since DRPs are one of the serious problems in cardiovascular diseases and many of them are preventable, the specific risk factors that facilitate the occurrence of DRPs are of considerable interest. Thus the objective of the study is to assess the risk factors for developing DRPs in patients with cardiovascular diseases.

DISCUSSION

Treatment regimen of cardiovascular disease is often complex in nature due to co-morbidities and severity of illness. According to a study, female gender, polypharmacy, administration of drugs with narrow therapeutic index, renal disease, age over 65 years and the use of oral anticoagulants and diuretics, were identified as relevant risk factors for ADEs and ADRs [6,14,15]. As per Leendertse and colleagues' study, poly-pharmacy, dependent living situation, four or co-morbidities, impaired cognition, impaired renal function and non-adherence to medication regimen, as independent and significant risk factors potentially responsible for preventable hospital admission[8].

Age:

Age is the major risk factor for cardiovascular diseases. Clinical manifestations and prognosis of CVDs likely become altered in older adults with advanced age because interactions occur between age-associated cardiovascular changes in health and specific pathophysiologic mechanisms that underlie a disease[16]. A fundamental understanding of age associated changes in cardiovascular structure and function is required for effective and efficient treatment of cardiovascular diseases in older persons[16]. Medicines and doses are often similarly prescribed in older and young patients. This is a main cause of DRP because pharmacological studies have shown for decades that many medications act differently in older and younger people due to the physiological and pathological changes that accompany ageing[17,18]. According to American Geriatrics Society (AGS), many medications have different efficacy and safety profiles in younger and older age groups[19]. The selection of medication, dosing schedules, and combined drug regimens, as well as appropriate follow-up and management of medication treatment, should always be age-specific and highly individualized among older

adults. Unfortunately, this is not a common clinical practice that makes the geriatric population more prone to DRPs [20]. Not only this, elderly patients are more susceptible and vulnerable to drug interaction and therapeutic dissatisfaction which might be due to age-related changes, for instance, changes in physiological, biological, physical and social functions [21]. A study found that advanced age is associated with high incidences of DRPs making it as one of the major risk factor for DRPs [22].

Female gender:

According to a study, females are more likely to develop DRPs than males. A prospective research study by R Adepu and P K Adusumilli found female population were having more DRPs than men [23]. This is because female patients being generally lighter in weight and smaller in build than their male counterparts but usually receiving the same drug doses had been demonstrated to be more prone to ADRs. This is probably attributable to the exposure to higher dose per body weight for the females than males [24].

Polypharmacy:

Polypharmacy is defined as the use of multiple medications and/or the administration of more medications than are clinically indicated, representing unnecessary drug use [25]. A study from Germany found that 78 % of the cardiovascular patients had been receiving more than four pills every day (median 8.34) [29]. In that most common products were beta-blockers (89 %), ACE-Inhibitors/Sartans (69 %) and aspirin (65 %) [26].

The risk of DRP is found to increase with the use of three or more drugs [27]. A cross sectional observational study found patients with poly-pharmacy were associated with increased risk of DRPs [28]. Not only this, they also found that the inpatients with mean length of hospital stay 5 days longer identified with at least one DRP than others [28]. In addition to this, they also observed hospitalized patients with CVDs were about 3 times likely to develop DRP than outpatients [27].

Another prospective study conducted by Paloma Gastelurritia and colleague revealed that, Heart failure (HF) patients are at high risk of experiencing Drug Negative Outcomes (DNOs) owing to polypharmacy, comorbidities, and old age [1,14,15]. The most frequently identified DRPs from their study were "insufficiently treated health problem" (31%), "inadequate dose, regimen, or duration of a drug" (22%), "probability of adverse effects" (16%), and "nonadherence" (14%). They also found a significant relationship between the number of DRPs and the number of drugs was found ($P < .013$) [1].

According to a cohort study by Gobezie Temesgen Tegegne and team, 96.1% of patients with cardiovascular diseases had one or more DRPs. Among them, need of additional therapy was one of the most common type of DRP [4]. Mekonnen AB found unnecessary drug therapy and need of additional therapy were the common DRPs in his study [29].

Multiple comorbidities:

Co-morbidities are the cause of increased mortality, decreased quality of life and increased use of healthcare services. A cross sectional study conducted in Netherlands revealed that cardiovascular disease patients have increased risk for comorbidity [30].

A cross sectional observational study conducted in large population of patients from a primary care registration network (RNH) revealed that, one CVD increases the risk of another, co-occurring CVD and a higher number of other chronic diseases such as lipid metabolism disorders, epilepsy, rheumatoid arthritis, thyroid disorders, diabetes mellitus and gout [30]. Kidney disease are often associated with CVDs as they are closely interrelated and disease of one organ cause dysfunction of the other, ultimately leading to the failure of both organs [31]. Patients with end-stage renal

disease (ESRD) are at much higher risk of mortality due to CVD [31].

Numerous studies have concluded that common DRPs in CVDs associated with kidney diseases are adverse events, drug interactions, and inappropriate doses [32,33,34]. These DRPs result from decreased kidney function which plays a major role in the elimination of drugs. The mortality rate associated with inappropriate drug use is 40% higher in CVD patients with an estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73m^2 compared with patients without CKD [35]. One more study found that CKD patients are poor adherent to pharmacotherapy, particularly cardiovascular medications [36].

A significant result was observed in a comparative study that showed that drug dosing adjustment service for elderly cardiovascular patients with renal impairment in community pharmacies can increase the proportion of adequate drug dosing, and improve DRPs per patient [37].

Drugs used to treat CVDs:

Cardiovascular diseases often require multiple medications to improve quality of patient's life, which can subsequently lead to complications. Numerous studies have concluded that cardiovascular medications are the most common drug class associated with the incidence of DRPs [38,39,40]. A large prospective study was conducted on adverse drug reactions in the United Kingdom reported that medications used to treat cardiovascular diseases such as anticoagulants, fibrinolytics, heparin, and diuretics were frequently implicated in causing adverse reactions [41].

A cross sectional retrospective study found that cardiovascular medications, particularly antiplatelet agents and lipid lowering agents, were associated with most cases of adverse reactions and drug-drug interactions [42]. The use of narrow therapeutic index drugs also contribute to DRP which is mainly due to lack of therapeutic monitoring [19].

DRP among cardiovascular diseases will lead health care professionals to optimize drug therapy that may influence health care cost, save lives, improves health, reduces morbidity and increases quality of life [43]. Awareness of factors carrying a high risk for DRPs, are important elements of drug therapy and may contribute to diminishing drug related morbidity and mortality. Early identification of the types and patterns of Drug Related Problems and the factors associated to them may enhance the prevention as well as management of DRPs. The prevalence of DRPs among patients with CVDs strongly supports the role of pharmacists in assuring patient safety [44]. Hence clinical pharmacy services must be improved to reduce the incidence of DRPs in cardiovascular patients.

CONCLUSION

DRPs in patients with CVDs have been linked to increased risk of negative clinical outcome. The main risk factors found from this study were female gender, polypharmacy, administration of drugs with narrow therapeutic index, renal disease, age over 65 years and the use of oral anticoagulants and diuretics and multiple co-morbidities. The effective clinical pharmacy services can reduce the incidence of DRPs in patients with cardiovascular diseases.

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