Cardiovascular Medicine Safety Profile Evaluation among Urban Private Hospitals

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Abstract

The pharmacovigilance is on-going, mandatory process among medical college hospitals. The private hospitals organization is prioritized and structured differently. Regular efficacy and safety evaluations are not conducted as academic research but occur by default in teaching hospitals. This study investigated and collected adverse drug reactions in this site and contrasted with literature from existing studies to draw comparisons and appropriate interventions.

This was a cross sectional observational study design using conventional ADR form from Central Drugs Standard Control Organization and checklist of cardiovascular medicine specific adverse reactions which was administered for data collection after necessary formalities for patient recruitment. There were statistically significant differences in total number of cardiovascular medications prescribed, the common cardiovascular medicines used, common concomitant medicine prescribed. The ADR profile showed commonly mild and moderate severity with low incidence of severe adverse event.

The adverse reaction profile did have large number of reactions but in the milder range. The cautious prescribing of large number of medicines with low intensity ADRs indicates the discharge of cautious responsibility due to direct liability and awareness. Peer misdemeanors among small circle of professionals would have severe repercussions on their clientele.

Introduction

Adverse Drug Reactions (ADRs) are one of the major factors that undermine the therapy. ADRs are unwanted medication effects that have a dramatic impact on economic and clinical perspective often leading to hospital admissions, prolongation of hospital stay and emergency department visits. Premarketing surveillances are conducted to detect and quantify ADRs. Randomized controlled trials have limited sample size and heterogeneity, ADRs occurs in real world during clinical practice rather than clinical trials. Thus post marketing medication safety monitoring including spontaneous reporting, observational studies helps in providing means of ADR detection, quantification and prevention [1].

Cardiovascular diseases are the most common cause of death globally. Every 36 seconds 1 person dies from cardiovascular diseases, and each day about 2500 in US are struck by Cardiovascular Disease (CVD) death overwhelms the death due to cancer, lung diseases, accidents and diabetes combined [2].

Most common cardiovascular diseases includes   coronary heart diseases, stroke, hypertension, congestive cardiac failure, myocardial infarction etc, generally treated with cardiovascular medications falling into classes of diuretics, anti-hyperlipidemics, beta-blockers, calcium channel blockers, ACE inhibitors, nitrates and anti-thrombotics.

Common ADRs for cardiovascular medicines includes hypotension, electrolyte imbalances, dry cough, pedal edema for anti-hypertensives and rhabdomylosis for statins. The ADRs increases the economic and clinical burden of the treatment [3,4].

This study aims to detect frequency rate, severity, and prevention of ADRs induced by cardiovascular medicines during the course of treatment.

Methodology

The design utilized in this study was of cross sectional-observational study, which was set up in two urban tertiary care hospitals with a sample size of 68.

Patients irrespective of their gender, age group between 30-90 years having history of clinical diagnosis of ischemic heart diseases, myocardial infarction, hypertension, angina pectoris, congestive heart failure were included and those with co-morbid condition of AIDS, severe infection and patients in I.C.U and I.C.C.U were excluded from the study .

Steps:

1.   Data collection forms were filled, from referring patient case file and patient interview.

2.   Observed ADRs were notified in ADR notification form.

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3.   Causality of the observed ADRs were assessed and documented.

4.   Results were analyzed by using Microsoft excel.

The information collected included, patient general data (initials, age, gender, height, weight), suspected ADR (brief description of the reaction, onset date v/s stop date of occurrence of events, outcome of events, treatment received), suspected medication (name, indication, start date, stop date, dose, frequency, route of administration), medical history (past and present), concomitant medications, and any other relevant history, including the pre-existing medical conditions.

Results

Total of 68 patients of mean age 64yrs were involved in the study and out of which male to female ratio were 1:1.

Commonest diagnosis were hypertension (80.8%), diabetes mellitus (54.4%), AWMI (10.2%), IHD (8%), followed by LVD (7.3%) (Figure 1).The commonest cardiovascular medicines prescribed includes antihyperlipidemics (64.7%) and Anti-anginal (54.4%) (Figure 2).The commonest ADR noted was anorexia (45.5%) and nausea (41.17%) (Figures 3-5). The correlation between number of cardiac medications and number of ADRs were found to 1, which is perfect correlation, positive linear relationship (Figure 6).

Discussion

In this study we explored the ADR profile occurring in cardiac patients among two urban private hospitals. The observations are noteworthy.

The study showed that the gender ratio was almost equal (1:1). The previous articles documented prevalence of ADRs during treatment with cardiovascular medications were common in women compared to men [5].

In a study of ADRs associated with anti-hypertensives by Khurshid et al. among the 192-hypertensive patients, 87 were males and 105 were females. A total of 21 ADRs were observed in 13 out of 192 hypertensive patients. Among the 13 patients reported with ADRs 8 patients were female and 5 were male. Females experienced more ADRs than males [6].

In study conducted by Hussain et al. in medicine OP department by questionnaire based patent interview a total of 34 adverse drug reactions were observed in 250 hypertensive patients during the four month study. A high percentage of adverse drug reactions occurred in middle aged and female patients and frequencies of ADRs were common in poly pharmacy than monotherapy [7].

In our study we have not used the Naranjo's scale for evaluating the ADRs which is the definite limitation of the study but this research was done to answer to the query of ADR occurrence in private sector hospitals.
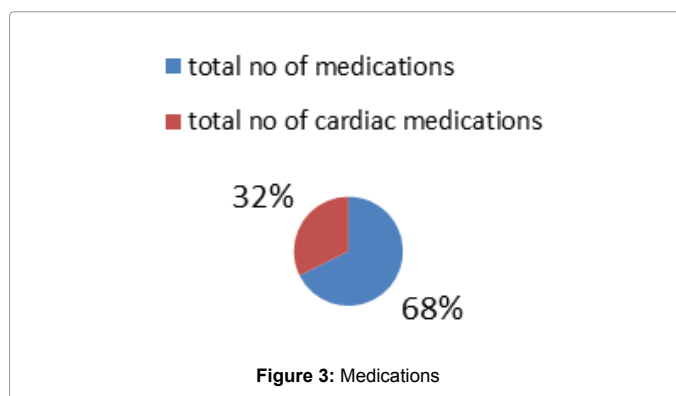
The mean age of subjects in our study is (64.46 ± 13.05).In the study by Rende et al. claims that most vulnerable age group for ADRs was > 61 yrs who have also been receiving multiple therapies .This high percentage is probably underestimated, because in older adults it may be difficult to recognize an ADR, as it can mimic some features of their age-related disease, Therefore, in elderly patients multiple therapies need to be discouraged, as these enhance the probability of ADRs, due to drug-drug interactions [3].

| Diagnosis	%
Diabetes mellitus type 2	54.4
Hypertension	80.8
Left ventricular dysfunction	7.35
Ischaemic heart disease	8.82
AWMI	10.29
COPD	5.8
LRTI	2.9
Hyperlipidemia	4.4
CKD	5.8
Stroke	1.4
Hypothyroidism	5.8
Hypercholestrolemia	4.4
PTCA	2.9
CAD	11.7

*AWMI: Anterior Wall Myocardial Infraction; COPD: Chronic Obstructive Pulmonary Disease;LRTI:LowerRespiratoryTractInfection;CKD:Chronic Kidney Disease;PTCA : Percutaneous Transluminal Coronary Angioplasty; CAD: Coronary artery Disease
Figure 1: Clinical diagnosis

Class of medication prescribed	%
Antihyperlipidemics	64.7
Beta Blockers	13.2
Ca^{2+} channel Blockers	29.4
ACE inhibitors	8.8
Diuretics	26.40
cardiac glycosides	5.80
drugs affecting blood	36.7
antianginal	54.4

Figure 2: Class of medication prescribed

Figure 3: Medications

Figure 4: Antibiotics

Figure 5: Frequency of ADRs observed
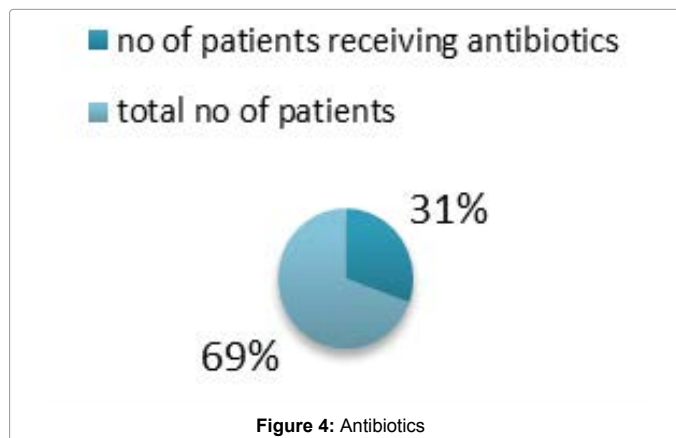
Figure 6: Correlation between number of cardiac drugs and no of ADRs
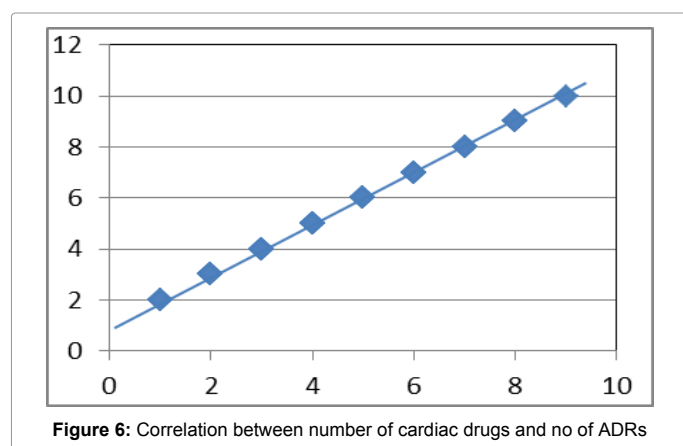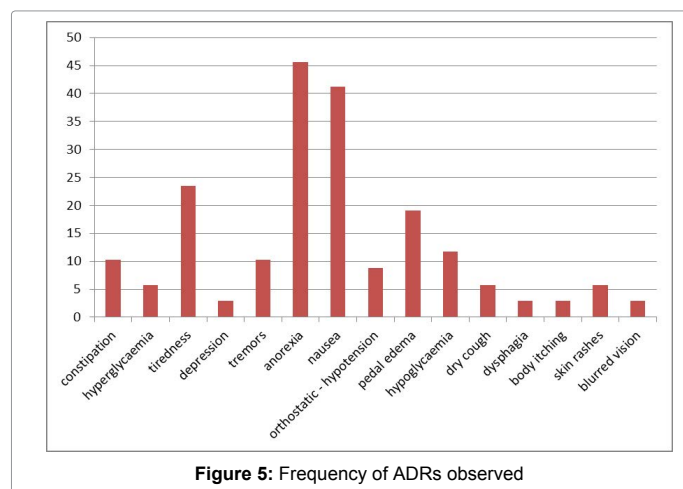
Study by Venturini et al. on gender differences, polypharmacy, and potential pharmacological interactions in the elderly, out of the 438 elderly patients in the data base, 376 (85.8%) used pharmacotherapy, 274 were female, and 90.4% of females used medications. Women younger than 80 years old used more medications than men in the same age group whereas men older than 80 years increased their use of medications in relation to other age groups [8].

In study by Sriram et al. in private tertiary care hospital, total of 57 documented ADRs were identified in 3117 General Medicine ward admissions during 12 months study period. The results of the age categorization revealed that the patients of 60 years and above age group experienced maximum ADRs which were about, followed by in age group between 30-59 years and 18-29 years age group [9].

Our study shows total number of medicines prescribed for a cardiovascular case is about 5.48, among which the cardiac medications are 2.6, on an average. Study by Venturini et al. The average number of medications used by each individual younger than 80 years was 3.2 ± 2.6 [8].

In our study Most common class of cardiovascular medicines received by the patient was anti-hyperlipidemics (54.4%), antianginal (45.5%), drugs affecting blood (36.6%), CCBs (29.4%), diuretics (26.4%).

In our study general ADRs observed during the treatment were anorexia (45.6%), nausea (41.17%), tiredness (23.52%), pedal edema (19.11%), hypoglycaemia (11.12 %), constipation (10.29%), tremors

(10.29%), orthostatic hypotension (8.8%), dry cough (5.8%). In study by Khurshid et al. calcium channel blockers (CCBs) was found to be the commonest therapeutic class associated with ADRs , followed by diuretics , β-blockers , ARBs and ACE inhibitors. CCBs associated with abdominal pain, ankle edema, sedation, pedal edema, and back pain. Diuretics with fatigue, visual impairment and dizziness. Dry cough was observed with ACE inhibitors [6].

In a study conducted on 19000 admissions in two National Health Services (NHS) units in UK 6.5% were due to ADRs [17].

In a study conducted on in-patients most frequent medications resulting in ADRs were opioid analgesics, antibiotics, diuretics, corticosteroids [18].

Study by Torpet et al. reported the occurrence of oral ADRs due to cardiovascular medications affecting oral mucous membrane, saliva production, and taste [19].

Study by Jimmy et al. shows that evaluation of patient characterization and reaction shows pattern of type A reactions were more common in elderly patients compared with other age groups and type B vice versa [20].

Study by Gallelli et al. on ADRs, NSAIDS was found responsible for 55.2% of ADR. Diclofenac and aspirin (acetylsalicylic acid) were the medications most frequently involved in the development of ADRs, while the skin was the body system most susceptible to NSAID-induced ADRs [10].

Study by Stern et al. suggests that calcium channel blockers are the cause for wide spectrum of cutaneous reactions like toxic epidermal necrolysis with diltiazem, Stevens-Johnson syndrome and erythema multiforme [12].

Study by Diaconu et al. shows that elderly patients prescribed with Diuretics are more likely to develop hypokalaemia and hyponatremia. Female patients had a higher frequency [13].

Study by Zafar et al. found that dry cough occurs with treatment by ACE inhibitors [15].

Study by Arumalni et al. found that the most common medications causing the ADRs were antibiotics associated with about one third of all the ADRs reported (55, 33.5%). Ampicillin produced the highest number of reactions followed by ciprofloxacin and nifedipine. Rashes were the most common ADR reported followed by edema, itching and diarrhoea. Skin was found to be the most commonly affected organ system followed by the central nervous and gastrointestinal systems [11].

Correlation analysis were done and value was found to be +1, which indicates that strong correlation exists between number of ADRs and number of cardiovascular medications in our study. The results of the study were limited by small sample size and geographical region.

Hospital admissions due to ADRs are significant health care problem in these days. As most of these reactions are predictable and preventable an awareness among health care professionals regarding detection, recording and reporting of ADRs following pharmacotherapy will prove to be very valuable for safer and rational drug utilization [14,16].

Conclusion

The present study is a part of Pharmacovigilance program conducted at two urban private hospitals, during this study safety profile

of commonly prescribed cardiovascular medications were evaluated and we observed the adverse reaction profile did have large number of reactions but in the milder range, it may be helpful in selection of appropriate treatments enhancing patient adherence, thus reducing unnecessary economic burden to the patients due to unwanted effects of the therapy. Also this study clearly indicates the number of adverse reactions reported with leading questions is definitely more than those by spontaneous reporting. We conclude that quizzing of the patient for various ADRs has a better reflection of ADR reporting than spontaneous.

References

1. Sultana J, Cutroneo P, Trifirò G (2013) Clinical and economic burden of adverse drug reactions. J Pharmacol Pharmacother 4: S73–S77.

2. Myerburg RJ, Kessler KM, Castellanos A (1993) Sudden Cardiac Death: Epidemiology, Transient Risk, and Intervention Assessment. Ann Intern Med 119: 1187-1197.

3. Rende P, Paletta L, Gallelli G, Raffaele G, Natale V (2013) Retrospective evaluation of adverse drug reactions induced by antihypertensive treatment. J Pharmacol Pharmacother 4: S47–S50.

4. Bruckert E, Hayem G, Dejager S, Yau C, Bégaud B (2005) Mild to Moderate Muscular Symptoms with High-Dosage Statin Therapy in Hyperlipidemic Patients-The PRIMO Study. Cardiovasc Drugs Ther 19: 403-414.

5. Mohebbi N, Shalviri G, Salarifar M, Salamzadeh J, Gholami K (2010) Adverse drug reactions induced by cardiovascular medications in cardiovascular care unit patients. Pharmacoepidemiol Drug Saf 19: 889-894.

6. Khurshid F, Aqil M, Alam MS, Kapur P, Pillai KK (2012) Monitoring of adverse drug reactions associated with antihypertensive medicines at a university teaching hospital in New Delhi. Daru 20: 34.

7. Hussain A, Aqil M, Alam MS, Khan MR, Kapur P et al. (2009) A pharmacovigilance study of antihypertensive medicines at a South Delhi hospital. Indian J Pharm Sci.71: 338-341.

8. Venturini CD, Engroff P, Ely LS, Zago LF, Schroeter G (2011) Gender differences, polypharmacy, and potential pharmacological interactions in the elderly. Clinics 66: 1867-1872.

9. Sriram S, Ghasemi A, Ramasamy R, Devi M, Balasubramanian R (2011) Prevalence of adverse drug reactions at a private tertiary care hospital in south India. J Res Med Sci. 16: 16-25.

10. Gallelli L, Colosimo M, Pirritano D, Ferraro M, De Fazio S et al. (2007) Retrospective evaluation of adverse drug reactions induced by nonsteroidal anti-inflammatory drugs. Clin Drug Investig 27: 115-122.

11. Arulmani R, Rajendran SD, Suresh B (2008) Adverse drug reaction monitoring in a secondary care hospital in South India. Br J Clin Pharmacol 65: 210-216.

12. Stern R, Khalsa JH (1989) Cutaneous adverse reactions associated with calcium channel blockers. Arch Intern Med 149: 829-832.

13. Diaconu CC, Balaceanu A, Bartos D (2014) Diuretics, first-line antihypertensive agents: are they always safe in the elderly? Rom J Intern Med 52: 87-90.

14. Subramanian M, Nadig P (2013) Adverse Drug Reactions in rural field pratice area of a teritiary teaching hospital. Int J Pharmacol Therapeut 3: 2-7

15. Israili ZH, Hall WD (1992) Cough and Angioneurotic Edema Associated with Angiotensin-Converting Enzyme Inhibitor Therapy: A Review of the Literature and Pathophysiology. Ann Intern Med 117: 234-242.

16. Palanisamy S, Kumaran K, Rajasekaran A (2011) A study on assessment, monitoring and reporting adverse drug reactions in an indian hospital. Asian J Pharm Clin Res 4: 112-116.

17. Pirmohamed M, James S, Meakin S, Green C, Scott AK et al. (2004) Adverse drug reactions as cause of admission to hospital:prospective analysis of 18 820 patients. BMJ 329: 15.

18. Davies EC, Green CF, Taylor S, Williamson PR, Mottram DR et al. (2009) Adverse drug reactions in hospital in-patients:a prospective analysis of 3695 patient episodes. PLoS ONE 4: e4439.

19. Torpet LA, Kragelund C, Reibel J, Nauntoft B (2004) Oral adverse drug reactions of cardiovascular drugs. Crit Rev Oral Biol Med 15: 28-46.

20. Jose J, Rao PG (2006) Pattern of adverse drug reactions notified by spontaneous reporting in an Indian tertiary care teaching hospital. Pharmacol Res 54: 226-233.