# Survey Of The Cardiovascular Drug Interactions On Geriatrics At Internal Medicine Ward Of RSUDZA Banda Aceh

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**Abstract**
The increase of elderly population in Indonesia leads to the drug misuse. The physiological change in geriatric become the major reason. It affects the change of      drug's pharmacodynamic, pharmacokinetics and the harmful drug interaction among overly prescribed medication. Cardiovascular drugs produce the most common side effect in elderly patient. This study aims to observe the accuracy of cardiovascular drugs used based on its dose and drug interaction. The subject of this study are the 60 years old-or more- inpatients in Rumah Sakit Umum Zainoel Abidin's (RSUDZA) Internal medicine ward who received cardiovascular drugs prescription. The data were collected from medical record and nurse's drugs record. The analysis were performed descriptively by evaluate the drug interaction theoritically based on literature study and available concensuses. The result shows that the Potential interaction occurred  in 75 ( 68.18 % ) of cardiovascular drug used, and 22 (20 %) of whom are important potential interactions. The most frequent drugs that have the potential interaction in this study are furosemide , spironolactone, captopril, digoxin and aspirin.
**Key words**: Drug interaction, Cardiovascular, Geriatric

## Introduction

Drug prescribtion in elderly becomes crucial due to their age-related  physical change such reduction of weight, albumin and body fluid, the increase of  body fat, and  alleviation of organ function. Those physical change affects the pharmacodynamics and pharmacocinetics of the drugs and indirectly affect the drug doses.  This condition leads to a misuse of drugs in elderly (Aronow, 2007, Finestone *et al.*, 2007). Epidemiological study shows that elderly patients are on the high risk of drug's side effect. Drug's side effect in 70-79 years old patient is seven times higher compared to 20-29 years old patient (Laroche *et al*, 2006). This incidence occurs due to polypharmacy practice among elderly. Polypharmacy is defined by the use of multiple drugs (more than 5 type of drugs)  in one periode of time. Several diseases that are commonly found in elderly patients causes the polypharmacy practice which is hard to be avoided. Some studies showed a positive correlation between the number of drugs that had been taken and  the high risk of side effect and drug interaction. In elderly patients who consume 10 type of drugs, the risk of  drug's side effect is more than 50% (Raza and Moyahed, 2002, Routledge *et al*, 2003). Cardiovascular drugs are the most common drugs that can cause side effect (Laroche *et al.*, 2006).

A survey in Indonesia showed 78%  of elderly suffered 4 diseases at the same time, 38% elderly live with 6 diseases and 13 % have 8 diseases (Rahmawati *et al.*, 2009). Another study in Sardjito Hospital in Jogjakarta (Rahmawati F *et al.*, 2006) stated that the highest risk drug interaction occurred in cardiovascular drugs.  Approximately 59%  elderly patients in hospital ward experienced the drug interaction from Furosemid, Captopril and Aspirin.  The use of cardiovascular drugs in Aceh is still not well-recorded. Therefore, our goal is to observe the accuracy of cardiovascular drugs prescription among elderly patients based on its interaction potency.

## Materials and Methods

This study is a descriptive study with cross-sectional design. The data were collected retrospectively from 50 medical records of the 60 years old-or more- patients in RSUDZA's internal medicine ward. The  interval of data collection ranged  from January 2014 to march 2014. The main data that were recorded are the identity (name, age, gender, weight, hospital admission date, out of treatment date, medical record's number), problems, diagnose, therapy (including dose, frequency, drug administrastion, duration of drug prescription, number of drugs that given), and      additional examination.  We compare the therapeutic data from medical records with the nurse record.  In case it is not in accordance with each other,  the nurse's record will be taken as the primary data.

The data were collected subsequently in a table and analyzed descriptively. The accurrary of drug administration was evaluated based on reference and recommendation from concensus and literature. Those concensus and litetature are: Pedoman Tata Laksana Penyakit Kardiovaskular di Indonesia/ Guidance of cardiovascular Treatment in Indonesia (2009), Goodman and Gilman's The

Pharmacological Basis of Therapeutic edisi 11 (2006), Martindale the Complete Drug Reference edisi 34 (2005), Drugs for the Heart edisi 6 (2005), dan Geriatric Dosage Handbook edisi 6 (2001).

**Results and Discussion**

This study was attended by 50 cardiovascular-drugs using patients. Among those number, 54% are male and 80 % are in between 60-74 years old (Table 1).

**Tabel 1**. Characteristic of Hospitalized Geriatric Patients

| Variables | Number of patients | % |
|---|---|---|
| **Gender** | | |
| Male | 27 | 54 |
| Female | 23 | 46 |
| **Age Group (years)** | | |
| 60-74 | 40 | 80 |
| 75-90 | 10 | 20 |
| > 90 | 0 | 0 |
| **The Number of medication prescribed** | | |
| < 5 | 11 | 22 |
| 5 – 9 | 29 | 58 |
| ≥ 10 | 10 | 20 |
| Total | 50 | 100 |

The total 344 drugs were used in all patients. In between, 110 drugs are cardiovascular drugs (Table 2). The range of used drugs per patient were 2-13 drugs. Most of them consumed 7 drugs.

**Table 2.** the percentage of cardiovascular drugs

| Type of cardiovascular drugs | n | Number of use Percentage (%) |
|---|---|---|
| Diuretic | 24 | 21,82 |
| Furosemid | 14 | 12,73 |
| Spironolacton | 6 | 5,45 |
| Hidroclorotiazid | 4 | 3,64 |
| **ACE inhibitor** | **9** | **8,18** |
| Captopril | 6 | 5,45 |
| Ramipril | 2 | 1,82 |
| Imidapril | 1 | 0,91 |
| **Angiotensin Receptor Inhibitor** | **24** | **21,82** |
| Valsartan | 10 | 9,09 |
| Candesartan | 13 | 11,82 |
| Telmisartan | 1 | 0,91 |
| **Calcium Channel Blocker** | **29** | **26,36** |
| Amlodipin | 29 | 26,36 |
| **Beta blocker** | **3** | **2,72** |
| Bisoprolol | 3 | 2,73 |
| **Heart Glikoside** | **3** | **2,72** |
| Digoksin | 3 | 2,73 |
| **Antiplatelet** | **14** | **12,73** |
| Aspirin | 10 | 9,09 |

| | | | |
|---|---|---|---|
| Klopidogrel | 4 | 3,64 | |
| **Anticoagulan** | **4** | **3,64** | |
| Warfarin | 2 | 1,82 | |
| Na enoksaparin | 2 | 1,82 | |
| **Total** | **110** | **100** | |

Amongst 110 cardiovascular drugs, there are 75 (68,18%) drugs which have interaction potency and 22 (20%) drugs which have to be restrictively supervised (Table 3). The type of drugs with potency of interaction are similar to other researches before such as furosemid, spironolacton, captopril, digoxin and aspirin. A study from Sardjito Hospital in Jogjakarta stated that there were 48 incidences of drugs interaction from 90 elderly patients in the ward. Among that number, 36 (75%) incidences involved cardiovascular drugs. The most common interaction of cardiovascular drugs in that study were furosemid, captoril, and aspirin (Rachmawati, 2006). Other study from Cipto Mangun Kusumo Hospital (RSCM) mentioned that in between 347 drugs (104 among them were cardiovascular drugs), 25 drugs (7,2%) had interaction potency and 18 drugs (72%) involved cardiovascular drugs. The most prominent interaction of cardiovascular drugs in this study come from captopril, furosemid, aspirin, and enoksaparin (Suardi, 2010). The high used of cardiovascular drugs that have interaction potency in those two researches indicate that the choice for cardiovascular drugs should be thoughtful and accurate in order to minimize the drug interaction. Drug interaction increases depend on age and the number of prescribed drugs (Midlov, 2009). This increase jumps exponentially. The interaction risk to the patient who consume 2 type of drugs is 6% but the risk jumps into 50 % in patients who consume 5 type of drugs and 100 % to the patient that consume 10 type of drugs (Lin, 2003).

In 2004, *the American Medical Directors Association* and *the American Society of Consultant Pharmacist* established a committee which was called by *Multidisciplinary Medication Management Project.* This committee aims to identify 10 type of the most cautious drugs among all drugs that used to be long-term prescribed to the elderly patient. Those drugs are warfarin–NSAID, warfarin–sulfa type antibiotics, warfarin–macrolid antibiotics, warfarin–cuinolon, warfarin–fenitoin, ACEi–Kalium, ACEi–spironolacton, digoxin–amiodaron, digoxin–verapamil, and teofilin–kuinolon (Brown, 2010). In brief, the cardiovascular drugs that have crucial interaction are warfarin, ACE inhibitor, spironolacton, digoxin, amiodaron and verapamil.

**Table 3**. The drugs with their potential drug interaction

| No | Drug I | Drug 2 | Mechanism of Interaction | Number of use |
|---|---|---|---|---|
| 1 | Furosemid | Aspirin | reduce diuretic's efication | 4 |
| 2 | Spironolacton | Captopril | elevate the risk of hipercalemia | 2 |
| 3 | Spironolacton | KSR | elevate the risk of hipercalemia | 1 |
| 4 | Spironolacton | Ramipril | elevate the risk of hipercalemia | 1 |
| 5 | Spironolacton | Imidapril | elevate the risk of hipercalemia | 1 |
| 6 | Captopril | Aspirin | reduce antihipertensi response | 2 |
| 7 | Captopril | Aspar K | reduce captopril absorbtion | 1 |
| 8 | Captopril | KSR | elevate the risk of hipercalemia | 2 |
| 9 | Ramipril | Aspirin | reduce antihipertensi response | 1 |
| 10 | Digoxin | Furosemid | elevate digoxin toxicity by hipocalemia | 1 |
| 11 | Digoxin | Bisoprolol | elevate inhibition of AV | 1 |
| 12 | Warfarin | Levofloxacin | elevate effect of warfarin anticoagulan | 1 |
| 13 | Clopidogrel | Omeprazol | reduce anticoagulan effect | 1 |
| 14 | Clopidogrel | Aspirin | elevate the risk of bleeding | 2 |
| 15 | Aspirin | Na enoksaparin | elevate the risk of bleeding | 1 |
| | Total | | | 22 |

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Warfarin oral anticoagulan has the possibility to develop Adverse Drug Reaction (ADR) due to the high drug interaction. Those risk are triggered by the narrow theurapetic index of Warfarin. In addition, warfarin's dose also needs to be individualized. Any change in other drug's dose can influence patient respons to warfarin. Severe bleeding often occur in 1-5 % cases per year with 25-30 mortality cases. (Ho LL *et al.*, 2002). This study exposed that the use of Warfarin was decline in the elderly. From 110 cardiovascular drug's user, only 2 patients used Warfarin. These two patient also shown the potency of interaction to other drugs that they consumed. Digoxin also has a high potency of interaction. In our study, there were 3 patients with digoxin treatment. Digoxin are known for its narrow therapeutic index. Digoxin's plasma concentration is not respectively described its effects and activities. Digoxin are recommended for small amount use with restrictive control due to its toxicity (Raza and Movahed, 2002). Patient with renal function alleviation are recommended to take a daily dose of 0.125 mg or interval one day dose of 0.125 mg digoxin (Ahmed, 2007).

Other drugs with the high risk of interaction are ACE inhibitor and Spironolacton. There are several conditions that can cause severe hiperkalemia in a heart failure patient with spironolacton, ACE inhibitor or AT1 Receptor Blocker (ARB) therapy. Those are elderly patient, consume more than 25 mg of spironolacton daily, alleviation of renal function and Diabetes mellitus type 2. Kalium's plasma concentration should be monitored periodically in these patients. Experts suggested to restrict the use of spironolacton to less than 25 mg a day or with the one day interval (Wrenger *et al.,* 2003)

Most of drug interaction could be predicted, avoided and minimized by a proper education about pharmacodynamic and pharmacokinetics. Therefore, the prescription of important cardiovascular drugs should not be stopped solely because of its potency of interaction. Alternative steps can be performed to handle the drug interaction effectively such as dose attenuation, high risk patient supervision, or treatment continuation if the drug effect is already in optimal dose or no clinically relevant interaction (Lin P, 2003, Hines L, 2008)

## Conclusion
Incidence of cardiovascular drug interaction in hospitalized geriatric patients in RSUDZA Banda Aceh was substantial. The Potential interaction occurred in 75 ( 68.18 % ) of cardiovascular drug used, and 22 (20%) drugs which have to be restrictively supervised. The most frequent drugs that have the potential interaction in this study are furosemide, spironolactone , captopril ,digoxin and aspirin.

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