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Research Article

PREDICTION OF RENAL IMPAIRMENT INDUCED BY STATIN THERAPY IN CARDIAC OUTPATIENTS

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ABSTRACT

Statin is the drug of choice to reduce the uncontrolled elevation of cholesterol. In Malaysia, about 90% of coronary heart patients use statins. Most of studies and reports on adverse drug reaction (ADRs) of statins based on doctors' assessments, few from patient's self-report. Objectives of this study are to determine the incidences in declining of creatinin clearance (CrCl) and renal ADRs induced by statin. Also, the risk factors of renal function disorders found during statin therapy. Cross-sectional and cohort retrospective design conducted for 345 patients of cardiac clinic at a general hospital in Northern part of Malaysia Peninsula. All patients in this study voluntarily participated by filling self-answer questionnaire. Validated questionnaire used to determine the renal ADRs induced by statins, while information of creatinin clearance (CrCl) collected from patients' progress files. Assessment of declining of CrCl depended on all patients' visits. Prediction analysis used to determine the risk factors. About 3% of patients suffered decline of CrCl less than 25% compared to baseline. The mean decline for all patients' visits was 12.6% ± 2.7%. Primary dyslipidemia contributed in declining of CrCl. The incidence of renal symptoms was 18.4% and 13.6% for dark urine and burning sensation in urination respectively. Indian patient had higher incidence of burning sensation in urination when compared to other races. In conclusion higher incidences of mild renal symptoms found in cardiac outpatients. Race and dyslipidemia type contributed higher decline of renal function. It recommended in reporting of the common urinary adverse reactions to reduce the incidence of renal dysfunction.

Keywords: Cardiac outpatient, Creatinine clearance, Adverse reactions, Indian, primary dyslipidemia.

INTRODUCTION

Statin is most common drugs use in Malaysia also throughout the world[1]. The range of statin use ranged from 62.5% to 91.7% of dyslipidemia patients, and the annual rate of statins use by cardiac patients is between 0.5% and 6.7%[2]. In Malaysia, about 90% of coronary heart patients use statins[3].

Most of studies and reports on adverse drug reaction (ADRs) of statins were based on doctors' assessments, and few from patient's self-report[4,5]. Few studies done related to the effect of statin on the renal function[6]. Eventhough, no study stated the correlation between the minor symptoms of statin and the renal dysfunction in longer duration use of statin. The objectives of this study were to determine common symptoms, the incidence of renal dysfunction, and the risk factors associated to the declining of renal function during statin therapy.

METHOD

Study design

The designs of this study were cohort retrospective and cross-sectional studies which conducted for 345 outpatients at cardiac clinic of a general hospital in Northern part of Malaysia Peninsula. This study approved by Hospital Ethical Committee and patients were voluntarily participated. Cross-sectional study based on validated questionnaires in assessment of the common ADRs associated with the renal dysfunction. The forms distributed over the duration of 5 months during cardiac clinic day. The total number of patients was 2000 during the study. Cohort retrospective study depended on the readings of renal laboratory data of the participants got from the patients' progress note.

Inclusion and exclusion criteria

Adult cardiac clinic patients over than 18 years old used statin and able to read Bahasa Malaysia or English language included in this study. Patients excluded were; allergic to statin, or changing the type and dose of statin. Also, preexisting renal insufficiency patients were excluded because they already have declining in creatinin clearance (CrCl).

Assessment of renal dysfunction

The renal dysfunction measured by reducing CrCl less than 25% of normal value. Determination of the risk factors based on a study done by Cannegieter[7].

Data Analysis

SPSS version 18 used to analyze the collected data, and Logistic regression, ANOVA, independent t test, paired t test and chi-square used. The statistical results which have p value less than 0.05 considered as significant outcomes.

RESULTS

Demographic data of the subjects

Majority of patients were males (63.5%), many of them were Chinese (44.8%) followed by Malay (34.4%), and Indian (20.8%), small percentages were smokers (15.6%) and alcohol consumers (18.7%). The mean age of the patients was 60 ± 10 years and the mean duration of satin used was 3.5-year.

Declining of renal function

The total percentage of patients had declining in CrCl was 3%. Percentage of patients had significant declining in CrCl was 1.15%, 3.10%, 13.5% and 8.3% in first, second, third, fourth respectively, as shown in Figure 1. The percentage of mean (±SD) decline in CrCl for these patients during all visits was 12.6%± 2.7% ($p < 0.05$).

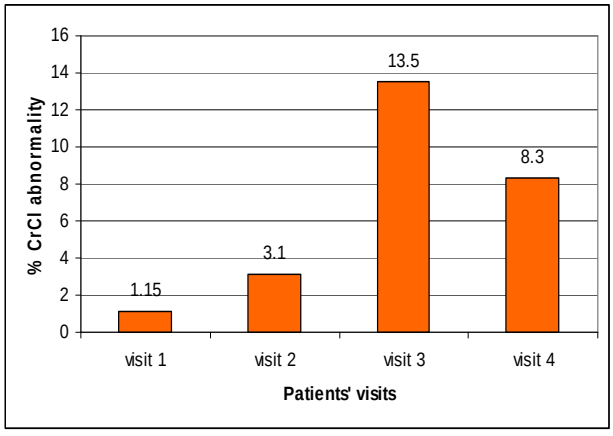

Fig. 1: Declining of CrCl with the increase of number of visits

Risk factors

Patient with primary dyslipidemia type got significant declining of renal CrCl. Indian patients showed higher sensitivity to the burning sensation in urination during statin therapy, as shown in Table 1.

Renal ADRs

The incidence of patients with dark urine and burning sensation in urination was 18.4% and 13.6% respectively. The incidence of mild, moderate and severe complaints for dark urine / burning sensation in urination was; 9.6%/12.6%, 2.8%/5.4%, and 1.2%/0.4%, respectively.

DISCUSSION

Depending on several previous studies, statins caused several serious renal function disorders[8-11]. Moreover, several adverse events caused by statins related to renal function like acute glomerulonephritis, nephritic syndrome, renal failure, and other diseases[12].

Table 1: Risk factors of the renal dysfunction in cardiac outpatients

Factors	Dark urine		Burning sensation in urination		CrCl < 25%	
	p value	OR	*p* value	OR	*p* value	OR
Gender (female)	NS	--	NS	--	NS	--
Race (Indian)	NS	--	**0.015**	**1.60**	NS	--
Smoking	NS	--	NS	--	NS	--
Alcohol consuming	NS	--	NS	--	NS	--
Type 1 dyslipid.	NS	--	NS	--	**0.003**	**3.50**
Duration (> 5 yrs)	NS	--	NS	--	NS	--
Age (> 65 yrs)	NS	--	NS	--	NS	--
Statin types	NS	--	NS	--	NS	--
Statin dose	NS	--	NS	--	NS	--
Combination therapy	NS	--	NS	--	NS	--
Medications	NS	--	NS	--	NS	--
Diseases	NS	--	NS	--	NS	--

Logistic regression used to predict the factors which contributed in the incidence of ADRs and declining of CrCl ($P < 0.001$)

In current study, 17 patients excluded from assessment because they had preexisting renal disease. Incidence of patients suffered to declining in CrCl by equal or more than 25% of their baseline was 3% for all patients' follow-up visits. This assessment followed by Cearfield et al[8] by determining the incidence of patients got serum creatinin less than 50% reduction compared to baseline, however as result no patient found with this assessment. While Mcaffe et al considered the renal dysfunction ranged between 1.5 ULN to double increase in serum creatinin[12]. The CrCl pattern showed decrease in renal function with an increasing number of visits. Significant decline found depending on follow up visits compared to baseline. The percentages of declines in CrCl were 8.61%, 13.82%, 15.90%, 12.44% and 12.61% for the second, third, fourth, fifth and sixth visits, respectively, compared to first visit. After calculations the declining mean of CrCl was 12.6% ± 2.7%.

As risk factors for renal function declining, no association found between declining of creatinin clearance and demographic data including gender, age, smoking and consuming of alcohol. Patients with primary dyslipidemia type had higher incidence of renal function declining than secondary. This because dyslipidemia types are differ depending on the raised phospholipids [13,14], and most of primary types suffered from elevation of low-density lipoprotein LDL. However, no significant difference found among primary or secondary types toward declining of CrCl. No significant contributions related to statin type, dose, combination therapy or duration of statin use. Also, no significant effect found for concurrent diseases and medication on declining of CrCl induced by statin.

High incidences of renal ADRs based on patients' complaints; 18.4% and 13.6% for dark urine and burning sensation during urination, respectively. For risk factors, race play role in declining of CrCl. FDA report showed that Asian patients are more sensitive to the ADRs than Caucasian patients because amount of statins in the blood will be two times higher in Asians than in Caucasians. In addition, there was a difference in the incidence of common ADRs, such as muscle pain, weakness, fever, nausea or vomiting[15]. In present study, Indian patients had higher incidence of renal ADRs for patients complaints when compared to others. Depending on previous literature statin symptoms with severe muscle pain, stiffness, weakness, fever, malaise and dark urine [16] and may suffer from renal failure[17].

This study showed that statins may consider as one of causes of renal problems in renal suffered cardiac patients. Significant difference found between the incidence of declining of renal CrCl (3%) and renal symptoms (18.4% and 13.6%). This because most of doctors are assessing the renal problems depending on the CrCl, neglecting the common unpredicted ADRs or their severity[18,19]. Although recent study stated that statin is renoprotective agent[20], but no information about renal function disorders in cardiac patients on chronic therapy. Reporting of adverse drug reactions depending on patients self-reporting is the proper method must be followed in determining the serious problems during therapy[21]. In conclusion darkening of urine considered as sign for renal dysfunction in patients with severe complaints, while mild cases more related to burning sensation in urination which can predict the renal function depending on the patients response. This study recommended the detection of dyslipidemia type and continuous reporting of the common urinary ADRs to reduce the incidence of renal dysfunction.

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