KSN 2020
FULLY VIRTUAL MEETING

Abstract Type : Poster
Abstract Submission No. : PO-1544

Fenofibrate-Associated Nephrotoxicity in Pateints with Chronic Kidney Disease

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Objectives:

Fenofibrate is widely used to treat hypertriglyceridemia for many years. It is well known that fenofibrate can trigger acute kidney injury. We studied to investigate the relationship between acute kidney injury and fenofibrate.

Methods:

We retrospectively evaluated the medical records of patients to start fenofibrate prescription for hypertriglyceridemia from January 2010 to December 2018 in the tertiary hospital. We reviewed their underlying disease, laboratory findings, dose of fenofibrate, duration of fenofibrate, and concomitant drug use. We did the effort to find factors related to acute kidney injury by fenofibrate.

Results: Total 267 patients were included. The mean age was 63.4 years old. 96 of 267 patients had acute kidney injury(36.0%). Patients with diabetes mellitus showed significantly increased risk of acute kidney injury without diabetes mellitus (27.7% vs 8.2%, p=0.009). We found significant correlation between hypertension and acute kidney injury. (27.3% vs 8.6%, p=0.005). Patients with concomitant use of RAS blockers showed significantly increased risk of acute kidney injury compared with non-use of RAS blockers(29.6% vs 6.4%, p=0.000).
72 of 195 patients had underlying chronic kidney disease(n=72, 27.0%). Mean estimated glomerular filtration rate(eGFR) by MDRD was each 46.6 ± 10.9 mL/min/1.73m² in chronic kidney disease group and 91.3 ± 23.7 mL/min/1.73m² in non-chronic kidney disease group. In subgroup analysis, patients with chronic kidney disease didn't have statistically significant risk of acute kidney injury by fenofibrate (12.0% vs 12.0%, p=0.079).

Conclusions:

Diabetes mellitus and concomitant use of RAS blocker have a statistically significant association with acute kidney injury by fenofibrate in our study. And patients with chronic kidney disease didn't have significant difference in risk in acute kidney injury by fenofibrate. We believe additional large-scale randomized controlled studies are needed.

Table 1. General characteristics of study populations

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		Total	AKI(n=96)	non-AKI(n=171)	p value
	Age	63.35	65.23	62.29	0.51
	WBC(x10³/μL)		7.33	7.47	0.666
	Hb(g/dL)		13.7	13.8	0.799
	BUN(mg/dL)		18.5	17.4	0.237
	Creatinine(mg/dL)		1.11	1.05	0.266
	Protein(g/dL)		7.09	7.14	0.515
	Albumin(g/dL)		4.36	4.38	0.723
	Sodium(mmol/L)		140.1	140.2	0.712
	Potassium(mmol/L)		4.65	4.55	0.168
	HbA1c(%)		7.57	7.15	0.073
	Triglyceride(mg/dL)		526.8	404.3	0.14
	Men(N,%)	196(73.4)	72(75.0)	124(72.5)	0.659
Comorbidities	DM(N,%)	179(67.0)	74(77.1)	105(61.4)	0.009
	HTN(N,%)	174(65.2)	73(76.0)	101(59.1)	0.005
	Liver disease(N,%)	12(4.5)	3(3.1)	9(5.3)	0.418
	Heart failure(N,%)	19(7.1)	10(10.4)	9(5.3)	0.116
	CKD(N,%)	72(27.0)	32(33.3)	40(23.4)	0.079
	Cardiovascular disease(N,%)	58(21.8)	22(22.9)	36(21.2)	0.741
	Malignancy(N,%)	8(3.0)	2(2.1)	6(3.5)	0.512
Concomitant drug	RAS blocker(N,%)	183(68.5)	79(82.3)	104(60.8)	0.000
	Metformin(N,%)	114(42.9)	42(43.8)	72(42.4)	0.825
	NSAID(N,%)	8(3.0)	3(3.1)	5(2.9)	0.933
	Furosemide(N,%)	16(6.0)	8(8.3)	8(4.7)	0.232
	Thiazide(N,%)	16(6.0)	8(8.3)	8(4.7)	0.232
	Other diuretics(N,%)	7(2.6)	3(3.1)	4(2.3)	0.700
	Statin(N,%)	207(77.5)	77(80.2)	130(76.0)	0.618

Multivariable logistic regression analysis for AKI associated with fenofibrate

Table 2. Multivariable logistic regression analysis for AKI associated with fenofibrate				
		OR	p value	95% CI
Comorbidities	**DM**	**1.971**	**0.029**	**1.074-3.617**
	HTN	1.414	0.366	0.667-2.995
	Liver disease	0.989	0.987	0.240-4.067
	Heart failure	1.902	0.252	0.634-5.708
	CKD	1.038	0.913	0.532-2.022
	Cardiovascular disease	0.985	0.965	0.495-1.959
	Malignancy	0.629	0.606	0.108-3.661
Concomitant drug	**RAS blocker**	**2.527**	**0.004**	**1.348-4.735**
	Metformin	0.645	0.228	0.316-1.316
	NSAID	0.866	0.863	0.170-4.416
	Furosemide	1.314	0.639	0.420-4.118
	Thiazide	1.573	0.415	0.529-4.673
	Other diuretics	0.910	0.907	0.185-4.468
	Statin	0.846	0.649	0.412-1.737