

Abstract Type : Oral

Presentation No. : OR 03 DO-09

Efficacy and Safety of Metformin in the Patients with Type 2 Diabetic Chronic Kidney Disease

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Objectives: Metformin is widely used as the best pharmacological option in the patients with type 2 diabetes mellitus. However, use of this drug has not been recommend in individuals with impaired kidney function because of the perceived risk of lactic acidosis. We aimed to assess the efficacy and safety of metformin in patients with type 2 diabetic chronic kidney disease (CKD).

Methods: We conducted a retrospective, observational, cohort study of 11,678 patients with type 2 diabetic CKD who followed the nephrology clinic at two tertiary hospitals from 2001 to 2016. We compared 3768 patients who used metformin with 7910 who did not use metformin. Primary outcome was defined as all-cause mortality. Secondary outcomes were kidney function, end-stage renal disease (ESRD) progression and event of lactic acidosis.

Results: The patients who used metformin had more female proportion, lower eGFR, and higher HbA1c level at the time of enrollment. Metformin-used group was better able to preserve kidney function. The all-cause mortality for metformin-used group was significantly better than that for non-metformin user in the multivariable cox analysis (P value <0.001 adjusted hazard ratio [aHR] 0.53, 95% confidence interval [C.I.] 0.45 - 0.62). Also, MFM group has longer duration of ESRD progression. (P value = 0.002, aHR 0.78, 95% CI 0.67 – 0.92). Also, there was no lactic acidosis event in both groups.

Conclusions: In Korean diabetic CKD patients, metformin could be safely used. However, more researches about how to use such as dose and monitoring are needed.

Demographic characteristics of cohort	ALL	MFM	non-MFM	p
No. of patients	11678	3768	7910	
Age (yr)	68.84 ± 12.862	67.93 ± 12.126	69.27 ± 13.177	0
HTN	5736 (49.1%)	1870 (49.6%)	3866 (48.9%)	0.446
Liver Disease	441 (3.8%)	109 (2.9%)	332 (4.2%)	0
Gender (Female)	6844 (58.6%)	2102 (55.8%)	4742 (69.3%)	0
BMI	24.14 ± 4.75	24.88 ± 5.60	23.77 ± 4.21	0
eGFR category (%)	11515	3704	7811	
>90	918 (8.0%)	427 (11.5%)	491 (6.3%)	
60 - 90	4128 (35.8%)	1666 (45.0%)	2462 (31.5%)	
30 - 59	3911 (34.0%)	1260 (34.0%)	2651 (33.9%)	
15 - 30	1220 (10.6%)	161 (4.3%)	1059 (13.6%)	
<15	725 (6.3%)	75 (2.0%)	650 (8.3%)	
ESRD	613 (5.3%)	115 (3.1%)	498 (6.4%)	
HbA1c first	7.37 ± 1.7 (n=11058)	7.58 ± 1.7 (n=3726)	7.26 ± 1.7 (n=7332)	0
HbA1c last	6.97 ± 1.3 (n=11061)	7.18 ± 1.3 (n=3726)	6.86 ± 1.3 (n=7335)	0
spot UPCR	2.9 ± 4.5 (n=1251)	2.8 ± 5.0 (n=684)	3.0 ± 4.0 (n=567)	0
spot UACR	211.5 ± 469.5 (n=1183)	222.8 ± 550.9 (n=639)	198.2 ± 350.5 (n=544)	0.267
Lactic max level	4.09 ± 3.6 (n=696)	3.78 ± 2.8 (n=180)	4.19 ± 3.8 (n=516)	0.192