

PLASMA α -DICARBONYLS PREDICT PROGRESSION OF CHRONIC KIDNEY DISEASE IN DIABETICS

Gina Iacovella-Alderson, Nathan L. Alderson, Hiroko Hama, David W. Ploth
Medical University of South Carolina, Charleston, SC

The incidence of diabetes is increasing in westernized societies with approximately 200 million cases world-wide. Approximately 30% of all diabetics will develop end stage renal disease (ESRD). Currently there are no reliable predictive tests for developing renal dysfunction.

The Advanced Glycation End-Product (AGE) / Advanced Lipoxidation End-Product (ALE) hypothesis predicts that irreversible chemical modifications of proteins are implicated in the pathogenesis of diabetic complications. The highly reactive α -dicarbonyls, glyoxal (GO) and methylglyoxal (MGO), are intermediates in both glycoxidation / lipoxidation reactions, processes which are accelerated in diabetics. We have previously demonstrated that treatment with dicarbonyl trapping agents prevented progression of nephropathy in rodents. Therefore it's hypothesized that plasma dicarbonyls may serve as biomarkers of protein modification in diabetics and thus predict those patients at highest risk for developing ESRD.

Age matched patients were assigned to one of three groups (n=6-8/group): Control (no history of diabetes or kidney disease); hyperglycemic and Stage III-IV CKD; hyperglycemic and Stage V CKD without dialysis. GFR (eGFR) was estimated using the modified MDRD equation. Plasma GO/MGO were quantified by GC/MS.

As shown below, plasma GO and MGO were significantly elevated in Stage III-IV (30% & 10%, respectively) and Stage V CKD (65% & 19%, respectively) compared to Controls. There was also a 25% increase in GO ($p < 0.02$) from Stage III-IV CKD to Stage V CKD. Additionally, there was no correlation between eGFR and plasma concentrations of GO/MGO. These data suggest plasma α -dicarbonyls may serve as independent predictors for CKD progression.

Group	GO (μ M)	MGO (μ M)
Control	104.3 \pm 9.3	33.4 \pm 0.62
Stage III-IV CKD	135.3 \pm 6.6 [*]	36.7 \pm 0.77 ^s
Stage V CKD	172.5 \pm 15.4 [#]	39.7 \pm 4.09 ^{&}

All values are mean \pm SEM

^{*} $p < 0.01$, ^s $p < 0.05$, [#] $p < 0.001$, & $p = 0.08$ vs Controls