Drug Dosing in Chronic Kidney Disease: Is the Cockcroft-Gault Formula Always the Best Estimator of Renal Function to Prevent Overexposure?

Introduction and Aims: Which creatinine-based GFR equation should preferentially be used in the context of drug dosing is highly debated. While most Nephrology guidelines recommend the use of the CKD-EPI equation, other specialists such as geriatricians keep on favoring the use of the Cockcroft-Gault equation (C-G). Along with the fact that dosing recommendations were most often initially done based on C-G, the main justification is that this equation usually provides lower value of GFR as compared to the CKD-EPI equation, and thus minimizes the risk of overdosing. Herein, we wanted to verify whether this assertion was systematically true regardless of demographic characteristics.

Methods: We developed a software program that explores, for different age strata and gender, more than 500 combinations of weight and serum creatinine values. For each combination, GFR was estimated by both CKD-EPI and C-G and the difference (CKD-EPI - C-G) was calculated. We considered a difference in eGFR between -10 ml/min and +10 ml/min as a good agreement between CKD-EPI and C-G. Alternatively, a difference below -10 ml/min and over +10 ml/min was considered as, respectively, a significant higher and lower GFR estimation given by C-G as compared to CKD-EPI.

Results: Overall, levels of agreement were significantly improved for the highest strata of ages with 36% and 62% of concordant GFR values for 40 and 80 years of age, respectively (p<0.01). For strata of ages above 70 years, C-G systematically gave lower GFR value for a weight below 60 kg and for a serum creatinine in the range of normal or near normal values. For weights above 90 kg, C-G-based values were never lower than CKD-EPI irrespective of the serum creatinine value. For strata of ages below 55 years, C-G provided significantly lower value of GFR in only less than 10% of the simulations.

Conclusions: Our data challenge the notion that C-G systematically gives lower value of GFR as compared to CKD-EPI. Age, weight and serum creatinine value are critical factors influencing the agreement between C-G and CKD-EPI. The typical situation in which C-G results in lower GFR estimates is a patient of 70 years old or more who tends to be underweight and with a low/normal serum creatinine value. Our data do not support the notion that disagreement between C-G and CKD-EPI should favor the use of C-G for preventing drug overdosing.