

DETERMINATION OF THE RENAL THRESHOLD FOR GLUCOSE EXCRETION IN FAMILIAL RENAL GLUCOSURIC PATIENTS

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Introduction:

The relationship between plasma glucose and renal glucose filtration, reabsorption and excretion is usually described as a threshold type.

Recently, a simple method to estimate the renal threshold for glucose excretion (RTG), using serial blood glucose sampling and urinary glucose collection in a standardized Mixed Meal Tolerance Test (MMTT) was validated for SGLT2 pharmacological inhibition in patients with diabetes mellitus type 2 (T2DM).

We have utilized this method to determine RTG in a small cohort of Familial Renal Glucosuria (FRG) patients.

Methods:

Seven subjects (six females) in two Nephrology units were enrolled

All subjects were screened for mutations in SGLT2

All underwent MMTT:

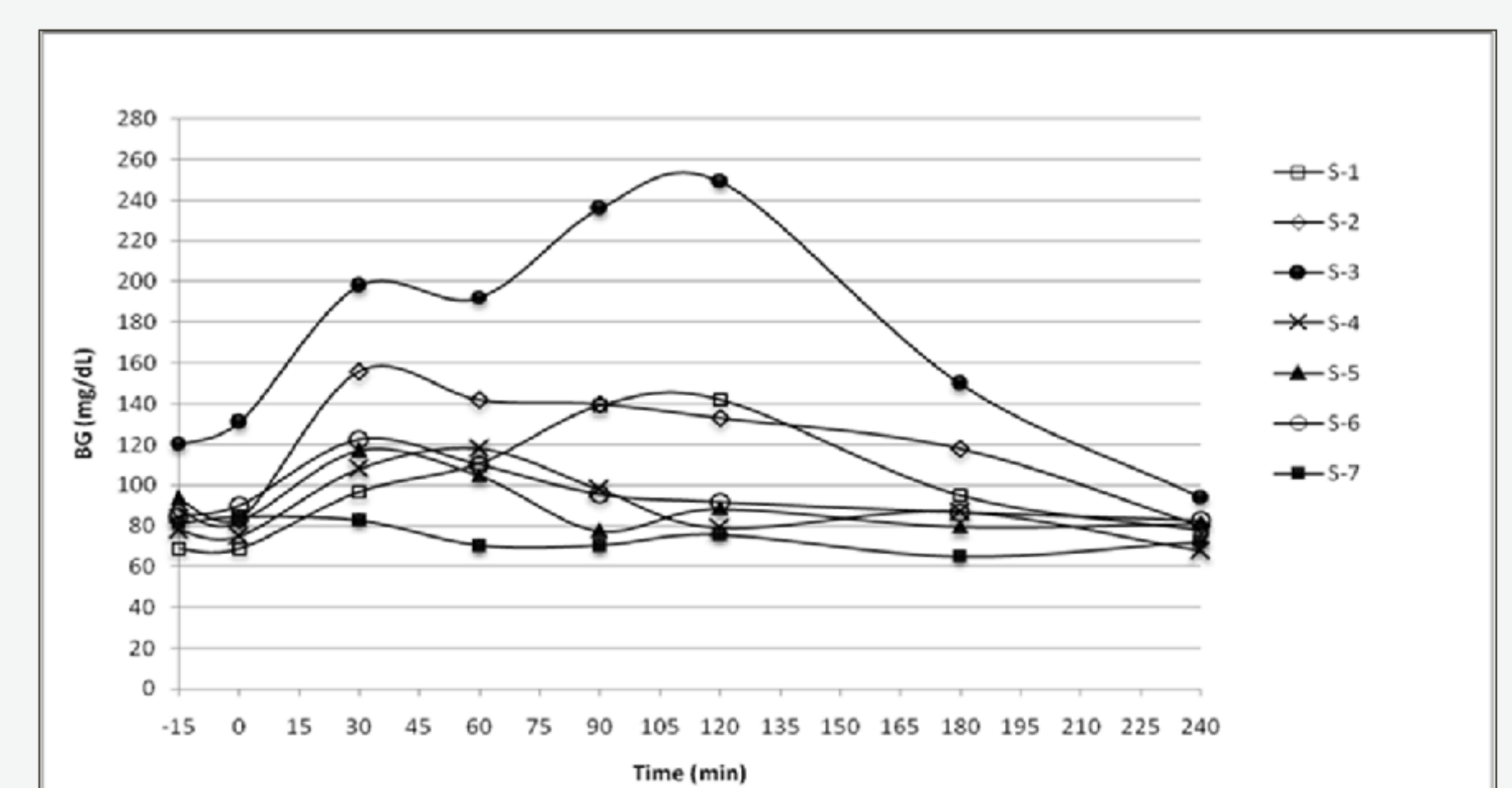
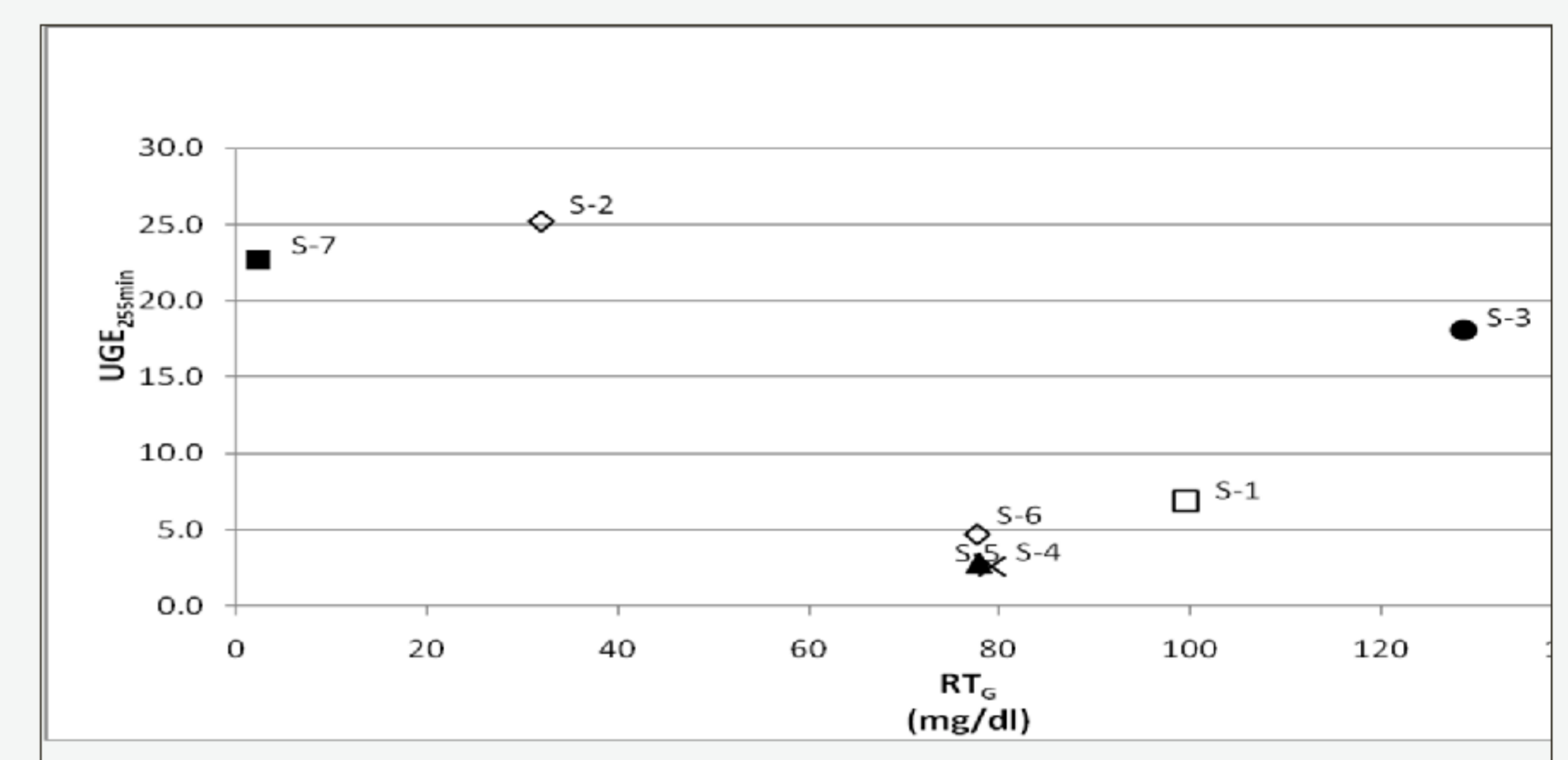
- Ingestion of a padronized meal (700 Kcal; 100g of CarboHidrates)
- Serial blood and urine collections for glycaemia and urinary glucose excretion (-15 to 240 minutes)
- GFR evaluation by MDRD formula (adult patients) or Schwartz formula (paediatric patients)

Plasma glucose and urinary glucose excretion were measured and used to calculate RTG.

Results:

Subject	Age (years)	BSA (m ²)	eGFR (ml/min/1.73m ²)	UGE _{24h} (g/1.73m ²)	UGE _{240min} (g)	UGE _{240min} (g/1.73m ²)	Fasting BG (mg/dl)	SLC5A2	RT _G (mg/dl)
S-1	59	1.63	91	16	6.5	6.9	88	IVS11-1g>a (heterozygous)	99.5
S-2	36	1.68	134	70.4	24.5	25.2	69	p.V346fsX17 (homozygous)	31.9
S-3	61	1.44	133	26.7	15.1	18.1	120	p.R558C (heterozygous)	128.6
S-4	31	1.48	89	2.8	2.2	2.6	78	p.C86R (heterozygous)	79.1
S-5	11	1.86	97.6	nd	3	2.8	93.7	p.L99fsX20 (heterozygous)	77.8
S-6	11	1.84	103.9	nd	5	4.7	84.7	p.L99fsX20 (heterozygous)	77.6
S-7	13	1.26	125.7	nd	16.5	22.7	81.1	p.C511S (homozygous)	2.2

- There was a high degree of variability of BG determinations during the test, therefore leading to different filtered glucose loads.
- Patient 3 was diabetic. She was included as glycosuria had been present before T2DM diagnosis and had excellent metabolic control. As expected, she had the highest BG during the MMTT.
- Considering UGE_{240min}, the highest values were found, as expected, in individuals homozygous for SLC5A2 mutations. The finding of an UGE_{240min} of 18.1 g/1.73m² in S3 heterozygous subject probably reflects her hyperglycemic condition.
- Homozygous patients had the lowest RTG values.



Conclusions:

- FRG individuals were shown to have a significant reduction in their RTG.
- Different alleles have different impact in the RTG.
- MMTT is a simple experimental procedure that characterizes more accurately, the impact of SLC5A2 mutations in the renal glucose transport.
- In the light of variable contributions of BG to the filtered glucose load, RTG is therefore a more precise tool to evaluate genotype/phenotype correlations than UGE

References:

De Fronzo, Diabetes Care 2013 ; Polidori D. J Clin Endocrinol Metab 2013

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