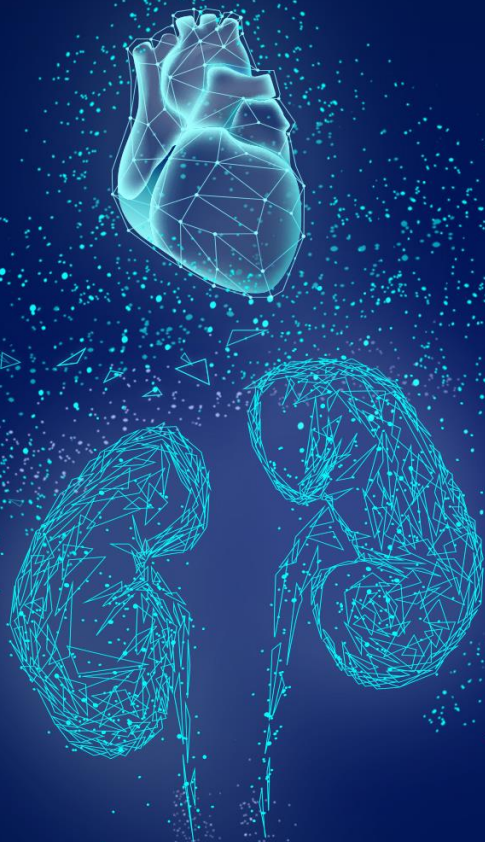


DM2 RENALITY

Nuevas dimensiones en enfermedad renal diabética.

ERA-EDTA HIGHLIGHTS

13-16 de junio 2019



Bicarbonato sódico retrasa la progresión de la ERC

Dra. María Marques

Con el patrocinio de:



Iniciativa científica de:



Subject Characteristics

Characteristic	Total (n=740)	Standard Care (n=364)	Sodium Bicarbonate (n=376)
	Mean (SD)	Mean (SD)	Mean (SD)
Laboratory characteristic			
Hemoglobin (g/dl)	12.3 (1.7)	12.4 (1.7)	12.2 (1.8)
Serum Albumin (g/dl)	3.9 (0.4)	3.9 (0.4)	3.8 (0.4)
Serum Glucose (mg/dl)	119 (41)	118 (41)	120 (40)
HbA1c (%)	6.7 (1.1)	6.7 (1.1)	6.7 (1.1)
Blood urea nitrogen (mg/dl)	94 (42)	86 (36)	101 (46)
Serum Creatinine (mg/dl)	2.3 (0.9)	2.1 (0.7)	2.4 (1.1)
Creatinine Clearance (ml/min)	30 (12)	32 (12)	28 (11)
eGFR (ml/min/1.73 m ²)	35.1 (11.8)	36.9 (10.8)	33.4 (12.4)
Serum bicarbonate (mmol/l)	21.5 (2.4)	21.4 (2.1)	21.7 (2.6)
Proteinuria (mg/day)	200 [69-400]	183 [0-310]	208 [100-555]

Study Intervention

Sodium Bicarbonate (SB) was administered twice daily to achieve a *target serum bicarbonate concentration of 24– 28 mmol/l* in the experimental group.

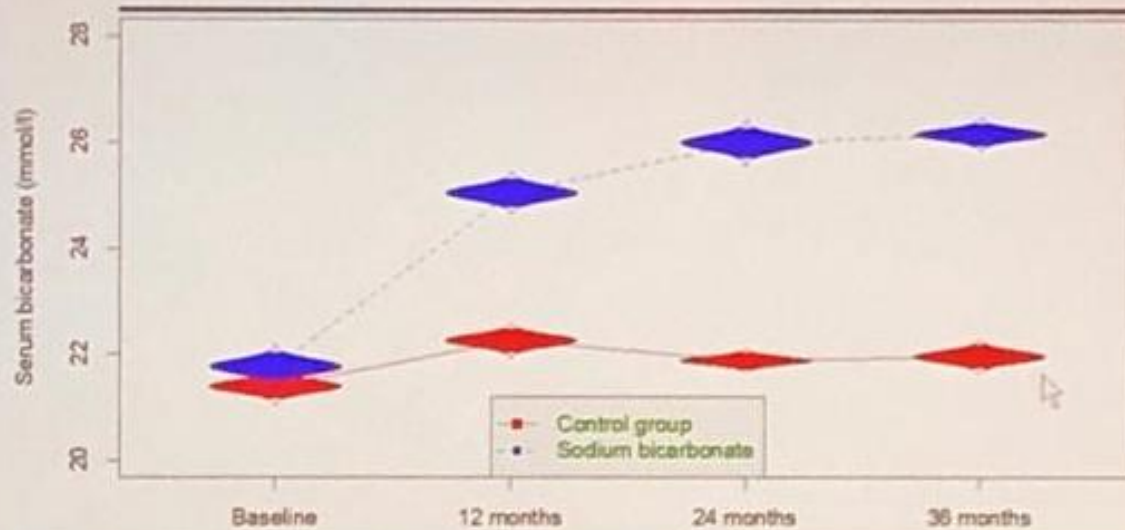
The starting daily dose was calculated to replace half of the bicarbonate deficit:

$$\text{bicarbonate deficit} = [24 - \text{serum bicarbonate (mmol/L)}] \times [\text{total body weight} \times 0.5]$$

The daily dose was subsequently increased by 25% every week until the serum bicarbonate target was achieved. The dose of SB was adjusted to keep serum bicarbonate levels <28 mmol/l as necessary.

RESCUE THERAPY WITH SODIUM BICARBONATE WAS ADMINISTERED TO SUBJECTS ALLOCATED TO STANDARD CARE AT PHYSICIAN DISCRETION

Serum Bicarbonate According to Study Treatment Allocation



1 mmol = 84 mg of SB

Dose: ~ 6.0 g/day
(Na⁺ ~ 1.6 g/day)
in 70 Kg subject

	Baseline	1 st year	2 nd year	3 rd year	P value*
Standard Care (SC)					
Mean (SD) SB administered dose (mmol/kg-bw/day)	-	0.28(0.23)	0.24(0.05)	0.21(0.06)	
Mean serum levels of bicarbonate (SD) (mmol/l)	21.4(2.1)	22.3(1.9)	21.9(1.3)	21.9(1.9)	<0.001
Range of serum bicarbonate (min-max) (mmol/l)	16-25	17-26	18-26	17-26	
Sodium bicarbonate (SB)					
Mean (SD) SB administered dose (mmol/kg-bw/day)	-	1.13(0.10)	1.12(0.11)	1.09(0.12)	
Mean serum levels of bicarbonate (SD) (mmol/l)	21.5(2.4)	25.0(2.4)	26.0(2.4)	26.1(1.7)	<0.001
Range of serum bicarbonate (min-max) (mmol/l)	13-26	20-29	21-30	22-30	
P value between group comparison	0,006	<0.001	<0.001	<0.001	

Primary Endpoint: Creatinine Doubling

Creatinine doubling (number of events N=87)			
	Hazard Ratio	95% Confidence Interval	p-value
Unadjusted	0.36	0.22-0.58	<.001
Model 1	0.36	0.22-0.57	<.001
Model 2	0.36	0.22-0.58	<.001
Model 3	0.36	0.22-0.57	<.001
Model 4	0.36	0.23-0.59	<.001

Model 1 adjusted for age and sex;

Model 2 adjusted for model 1 and demographics, body mass index, and blood pressure

Model 3: adjusted for model 2 and comorbidities (renal function, cardiovascular disease, peripheral arterial disease, diabetes, hypertension)

Model 4: adjusted for model 3 and proteinuria, use of renin-angiotensin-aldosterone system inhibitors

Safety endpoints according to study allocation

Blood pressure control	Sodium Bicarbonate			Standard Care		
	Baseline	Follow-up	p-value*	Baseline	Follow-up	p-value*
Mean Systolic Blood Pressure mm Hg (SD)	129 (19)	127 (16)	0,147	128 (18)	127(15)	0,423
Mean Systolic blood pressure change mm Hg	-1.5 (19.8)			-1.2 (10.9)		0,086
Mean Diastolic Blood Pressure mm Hg (SD)	73 (8)	74 (9)	0,202	74 (11)	76(10)	0,001
Mean Diastolic blood pressure change mm Hg	-3.0(11.0)			-2.5(10.1)		0,037
Prevalence of systolic blood pressure N (%)	Baseline	Follow-up	p-value	Baseline	Follow-up	p-value
>145 mm Hg	53 (23.3)	36 (11.0)	0,001	86 (25.7)	52 (15.6)	0,001
135-145 mm Hg	51 (15.6)	49 (15.0)	0,916	34 (10.2)	61 (18.3)	0,004
<100 mm Hg	32 (9.8)	19 (5.8)	0,077	17 (5.1)	11 (3.3)	0,01
Prevalence of diastolic blood pressure N (%)	Baseline	Follow-up	p-value	Baseline	Follow-up	p-value
>85 mmHg	28 (8.6)	25 (7.6)	0,743	10 (3.0)	8 (2.4)	0,814
Nutritional parameters	Baseline	Follow-up	p-value	Baseline	Follow-up	p-value
Serum Albumin (g/dl)	3.8 (0.4)	3.9 (0.4)	0,005	3.8 (0.4)	3.8(0.5)	0,778
Serum Hemoglobin (g/dl)	12.2(1.8)	12.4 (2.1)	0,499	12.4 (1.7)	12.3 (1.8)	0,482
Serum potassium (mmol/l)	4.9(0.5)	4.9(0.6)	0,518	4.9(0.6)	4.9(0.7)	0,487
24 hours urine sodium (mmol/l)	157 (41)	154 (23)	0,384	173 (44)	159 (41)	0,001
24 hours chloride (mmol/l)	128 (22)	98 (21)	0,001	124 (20)	119 (24)	0,04
Body weight (Kg)	74.7(13.0)	74.0 (11.7)	0,467	75.6 (9.7)	74.9(11.7)	0,282

Safety endpoints according to study allocation

	First Year	Second Year	Third Year	
Standard Care				p value for trend
Number hospitalized	92	81	84	0.086
Proportion hospitalized (%)	26,6	33,6	34,6	
Number of days in the hospital	1085	975	1160	
Sodium Bicarbonate				p value for trend
Number hospitalized	101	38	35	0.037
Proportion hospitalized (%)	29,7	15,4	14,2	
Number of days in the hospital	1168	422	400	

Summary

In conclusion, correction of metabolic acidosis with oral sodium bicarbonate is safe and reduces the risk of CKD progression and all-cause mortality in patients with CKD.



Acknowledgment: We thank the doctors, nurses, and administrative staff who assisted in conducting the UBI Study project. All costs connected to the UBI Study were covered by the Italian National Health Care System and an unconditioned grant offered by the Italian Society of Nephrology.

On behalf of UBI Study Group (in alphabetical order): Vincenzo Barbera (Colleferro), Annamaria Bruzzese (Messina), Valeria Canale (Messina), Giuseppe Conte (Napoli), Vincenzo Crozza (Ariano Irpino), Adamasco Cupisti (Pisa), Antonella De Blasio (Caserta), Emanuele De Simone (Avellino), Lucia Di Micco (Solofra), Fulvio Fiorini (Rovigo), Rachele Grifa (San Giovanni Rotondo), Raffaella Nardone (Salerno), Matteo Piemontese (Foggia), Maria Luisa Sirico (Solofra), Fabio Vitale (Ariano Irpino)