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Randomized Clinical Study, Comparative of Parallel Groups, to Evaluate the Effectiveness of Three Preparations of Potassium Citrate in Producing an Increase in Urinary pH in Patients with a History of Kidney Stones

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Abstract

Background: A very strict control of urinary pH is recommended to maintain it between 5.5 and 6.2, preventing formation or recurrence of crystals. Kidney stones are a common problem, with a high rate of recurrence, not altered by the success of surgery. Medical treatment prevents recurrence. Potassium Citrate inhibits crystallization of calcium salts. It influences calculogenesis by increasing urinary citrates and alkalinizing the urine. **Purpose:** to evaluate the similarity in the effect of three K citrate products, K citrate reference product Urocit® 10 mEq, and K citrate from Laboratorios LETI S.A.V., 10 mEq and 15 mEq, on urinary pH. **Materials and Methods:** We carried out a prospective, randomized study of three parallel groups. We admitted female and male patients with history of kidney stones or evidence of lithiasis (grit, microlithiasis) in the renal echosonogram. Laboratory assessments: urine, 24-hour urine, urinary pH, Calcium, uric acid, Phosphorus, Sodium, protein and urinary creatinine at times: start, day 7, day 21, 30 of treatment. **Results:** all three products produced a slight increase in urinary pH in the simple urine test and 24-hour urine, with no differences between groups or their logarithmically transformed means and their CI95, which did not exceed the range between 80% and 125%. **Conclusions:** K Citrate, 10 mEq and 7.5 mEq, from Laboratorios LETI, S.A.V., at a dose of 30 mEq daily in patients with history of kidney stones are equivalent to the reference product Urocit®, in its effects on urinary pH in 24-hour urine, and in the simple urine test.

Keywords

Nephrolithiasis, Potassium Citrate, Urine pH, Pharmacodynamic Equivalence

1. Introduction

Kidney stones continue to be a very common problem. Its diagnosis and prevention have not decreased its frequency, with a high rate of recurrence that is not altered by the success of surgery. There is currently ample evidence that medical treatment does prevent recurrence, which is why pharmacological treatment has been returned.

Citrate has received great interest in the study and prevention of kidney stones, mainly due to its powerful inhibitory action on the crystallization of calcium salts, and is currently the best studied non-organic inhibitor. The recommended dose is 30 - 100 mEq/day, depending on the level of citraturia to be corrected. Doses greater than 30 mEq/day should be divided into 2 to 3 daily doses [1].

Renal lithiasis has an incidence of 10% in industrialized countries, it is three times more common in men, recurrence occurs in 40% to 50% in the first five years and recurrence intervals become shorter [2].

Citric acid is a tricarboxylic acid with a pK of 5.6; therefore, at physiological pH more than 90% is found as trivalent anion. Plasma citrate concentration is low, 0.14 mmol/l (2.4 mg/dl), varies between 0.05 and 0.3 mM and circulates largely in complexes with sodium (Na), calcium (Ca) and magnesium (Mg) and very little bound to large molecules, thus more than 90% of plasma citrate is freely filtered by the kidney [3]. Plasma citrate is endogenous, its main sources being bone and intermediate liver and muscle metabolism. Its plasmatic levels seem to be quite independent of the diet, because once the citrate from food is absorbed, it is rapidly metabolized in the liver. However, if an oral citrate load, for example, a citrate salt, is given, its plasma levels transiently increase [4]. At the intracellular level, it is a central component of the Krebs cycle, that is, it is an energy donor. Citrate is mainly used by two organs, liver and kidney [4]. At the urinary level, it is a powerful inhibitor of the crystallization of calcium oxalate salts (OxCa) and calcium phosphate (PCa); therefore, hypocitraturia is a risk factor for calcium stone formation [5] [6].

Citrate, primarily the divalent citrate species, binds to Ca^{2+} in the urine and forms a soluble salt, calcium citrate; on the other hand, by reducing Ca^{2+}, it manages to reduce urinary saturation with respect to OxCa (Calcium Oxalate) and PCa (Calcium Phosphate) [6] [7] and directly inhibits the crystallization of OxCa and PCa [4]. It has also been shown to inhibit spontaneous OxCa precipitation [7] and monosodium urate-induced OxCa nucleation [8].

It is a potent inhibitor of the aggregation of preformed OxCa crystals [9], especially the trivalent species. It binds to the surface of crystals and forms an Ox-

Ca-citrate complex, preventing crystal aggregation. The importance of this action lies in the fact that crystal aggregation plays a critical role in the process of stone formation.

Systemic, tubular, and intracellular pH is the factor that most affects citrate excretion; acidosis decreases its excretion while alkalosis increases it. Small decreases in tubular pH (7.4 to 7.2) significantly increase its tubular reabsorption.

The use of potassium citrate (K citrate) in the prophylaxis of kidney stones did not begin, however, until 1985, when the US Food and Drug Administration approved it under certain conditions [10].

The therapeutic effect of potassium citrate on calculogenesis is due to the increase in urinary citrates and its alkalinizing action. A second protective effect of citrate on calculogenesis is due to its inhibitory effect on the crystallization of calcium oxalates and phosphates, inhibiting nucleation. Spontaneous formation of these calcium salts and the heterogeneous nucleation of calcium oxalate on urates, delaying the agglomeration of existing calcium oxalate crystals and inhibiting the growth of calcium oxalate and calcium phosphate crystals. Finally, the third effect of citrate derives from the elevation of urinary pH, which increases the amount of dissociated uric acid and the formation of alkaline urates in the urine, preventing the formation of uric acid stones or redissolving those already formed; it also prevents the formation of uric acid crystals that could act as very effective heterogeneous nucleators of calcium oxalate [11] [12].

LETI Laboratories has developed a modified release formulation of K citrate in tablets of 10 and 7.5 mEq, which must be compared with the reference product Urocit® 10 mEq, approved in the country, to demonstrate that they are equivalent in their effect on the urinary pH.

Potassium Citrate 7.5 and 10 mEq, LP Tablets from LETI Laboratories, are prolonged-release products in the form of white, oblong-shaped, coated tablets. Its active ingredient is Tripotassium Citrate Monohydrate, which provides 7.5 or 10 mEq (respectively) required for the dose to be administered. The nature of the design is of the polymeric matrix type that generates, when hydrated, a gradual release of the active ingredient for up to 5 hours, providing the patient with the desired effect as urine alkalinizer in the treatment of Renal Lithiasis. The tabletsare covered by a polymer layer that guarantees easy swallowing of the tablet by the patient. [13].

Definitively, the desired benefit with the administration of potassium citrate in patients with kidney stones is to achieve an increase in urinary pH that produces a decrease in urinary calcium and its crystallization [11] [14] [15].

Taking into consideration that it is the increase in urinary pH that determines the final therapeutic action of the product, this study was carried out in order to compare three formulations of K citrate with modified release. The aim was to demonstrate equivalence in their effect on pH and, therefore, on their ability to reduce the production of kidney stones, comparing their ability to modify urinary pH in patients with a history of kidney stones.

1) Objectives: to evaluate the similarity in the effect of three potassium (K) citrate products, K citrate reference product Urocit™ 10 mEq, and K citrate from Laboratorios LETI S.A.V, 10 mEq and 15 mEq, on urinary pH.

2) Materials and methods: We conducted a prospective, randomized study of three parallel groups.

Inclusion criteria

1) Stone-forming patients.

2) Patients aged between 18 and 85 years.

3) Patients with a history of kidney stones.

4) Patients who present evidence of lithiasis (grit, microlithiasis) on the renal echosonogram.

5) Patients who have signed a written consent that they have been sufficiently informed about the study and that they agree to participate in it.

Exclusion criteria

1) Patients in treatment with drugs prohibited in this study: Macromolecules: Glycosaminoglycans: Citrate, Phytate, Tartrate. Amino acids: Aspartic, Glutamic, Alanine, Magnesium, Pyrophosphate, Trace elements.

2) High levels of potassium in the blood (hyperkalemia), the normal range is 3.7 to 5.2 mEq/L.

3) Patients with hypercalcemia (Normal values range from 8.5 to 10.2 mg/dL (2.13 to 2.55 millimole/L).

4) Urinary tract infection.

5) Patients with diarrheal syndrome.

6) Previous diagnosis of Addison's disease (adrenal gland).

7) Soft tissue injury or acute burn.

8) Diagnosis or history of peptic ulcer.

9) Dehydrated patients.

10) Patients taking a "potassium-sparing" diuretic such as amiloride (Midamor, Moduretic), or spironolactone (Aldactone, Aldactazide), triamterene (Dyrenium, Dyazide, Maxzide).

11) Creatinine > 1.5 mg/dL.

12) History of metabolic alkalosis or conditioning diseases of said pathology.

13) Patients receiving anticholinergic therapy.

14) Intestinal obstruction.

15) Treatment with: Angiotensin converting enzyme inhibitors, Angiotensin AT1 receptor antagonists, indomethacin, sodium bicarbonate or other preparations containing potassium and treatment with thiazides or allopurinol.

16) Uncontrolled arterial hypertension SBP ≥ 140 mmHg and DBP ≥ 90 mmHg.

17) Previous diagnosis of myocardial infarction within six months prior to the start of the study.

18) Previous diagnosis of cerebrovascular accident of any type within the six months before the start of the study.

19) Patients with a previous diagnosis of asthma or with COPD.

20) Cardiac arrhythmias of any kind as background, or identified in the research doctor's office through physical examination.

21) Acute dehydration.

22) Gastric emptying disorders.

23) Congestive heart failure > Grade I NYHA.

24) Presence or suspicion of pregnancy, ruled out, if suspected, by blood determination of the β fraction of human chorionic gonadotropin.

25) Breastfeeding patients.

26) Severe liver function disorders (liver enzymes 3 times above their normal value).

27) Previous diagnosis of peripheral arterial vascular disorders.

28) Patients taking birth control pills (patients of childbearing potential should avoid pregnancy by using a barrier method, intrauterine device, or being surgically sterilized).

29) Poorly controlled diabetes (basal blood glucose greater than 126 mg/dL or glycosylated HB greater than 7%). Diabetes care volume 40 Suppl 1 January 2017, Glycemic Targets pg S50.

30) History of alcohol abuse.

31) Drug abuse, defined as excessive, persistent, or sporadic use of drugs that is not consistent with or related to acceptable medical practice.

All patients signed a written consent indicating that they had been sufficiently informed about the study and that they agreed to participate in it. The study was approved by an institutional ethics committee and by the National Regulatory Authority (approval JRPF-0307-2017).

The purpose of the study was explained to the patients. Upon accepting their participation, they signed the Informed Subject Consent and were randomly assigned to one of the three (3) groups. Two of the groups were instructed to receive potassium citrate at a dose of 10 mEq (one 10 mEq tablet) three times a day for 30 days; a third group was assigned to receive the Leti Potassium Citrate formulation (two 7.5 mEq tablets) twice daily for 30 days.

At the beginning and at the end, laboratory tests were performed (complete blood count, blood glucose, glycosylated hemoglobin, urea, creatinine, transaminases, triglycerides, total cholesterol, HDL cholesterol, LDL cholesterol, electrolytes, urine); at the times: start, day 7, day 21 and 30 of treatment, urine, 24-hour urine with determination of pH, Calcium, uric acid, Phosphorus, Sodium was performed. (Neither citrate nor oxalate could be determined because these reagents were not available in the country at the time of the study).

The formula used to calculate the size of the samples is based on the development presented by J. Fleiss[1] taking the pH data from the study: Reference values of urinary citrate and oxalate for inhabitants of the metropolitan area of Anzoátegui State, Venezuela, Interscience, vol. 26, No. 3, March, 2001, p. 122-125.

[1]Fleiss, J. The design and analysis of clinical experiments. Statistical methods for rates and proportions. John Wiley & Sons, 1986, p. 432.

According to the calculations, with 15 patients per group (3 groups) we could analyze the urinary pH and demonstrate a difference in pH of 10%.

2. Results

We admitted 47 patients in the study, of which only 46 entered the analysis because one patient violated protocol and was admitted with a urinary tract infection.

There were statistically significant differences (*) in the parameters: weight, height, body mass index and SBP, without clinical significance, as seen in Table 1.

Given that the only difference detected between the groups K Citrate Ref., 10 mEq and K Citrate TEST 10 mEq were observed on day 30 of treatment, the confidence intervals were analyzed to determine if the difference between the means included the intervals (Table 2).

Neither for the pH data, or its logarithmic transformation, the means or the confidence intervals are far from the established limits of Bioequivalence 80% - 125%: Mean: 105%, CI min: 102.1%, CI max 107, 8%.

The other variables measured in the simple urine test: glucose, ketones, proteins, leukocytes, cylinders or bacteria did not show significant changes. In some patients, the number of red blood cells was increased by the presence of menstruation.

Neither the means nor the CI are below 80% or above 125% (Table 3 and Table 4).

Table 1. Description of the evaluated population.

Parameter	Potassium citrate (Ref) 10 mEq	Potassium citrate (Test) 10 mEq	P between Ref. and Test (10 mEq)	Potassium citrate (Test) 15 mEq	P between Ref. and Test (15 mEq)
Age (years)	43.7 ± 15.3	36.6 ± 12.3	0.17	45.1 ± 12.9	0.79
Sex (f/m)	8/7	6/9		13/3	
Weight (kg)	65.4 ± 12.7	74.0 ± 13.5	0.08	73.06 ± 25.9	0.00*
Height (m)	1.62 ± 0.1	1.67 ± 0.1	0.11	1.63 ± 0.1	0.00*
BMI	24.8 ± 3.9	26.5 ± 4.3	0.24	25.48 ± 9.3	0.00*
SAP (mmHg)	118.1 ± 12.4	118.1 ± 10.4	1	117.5 ± 12.9	0.00*
DAP (mmHg)	73.9 ± 8.8	75.4 ± 6.7	0.6	73.1 ± 8.7	0.79
Evaluation of symptoms					
Pain	0	0		0	
Macroscopic hematuria	0	0		0	
Alterations in physical exam	0	0		0	

Table 2. pH in simple urine test.

Time	Potassium citrate (Ref) 10 mEq	Potassium citrate (Test) 10 mEq	P between Ref. and Test (10 mEq)	Potassium citrate (Test) 15 mEq	P between Ref. and Test (15 mEq)
Beginning	5.81 ± 0.6	5.18 ± 1.6	0.17	5.73 ± 0.5	0.69
Day 7	5.73 ± 0.7	5.66 ± 0.7	0.78	5.97 ± 0.6	0.37
Day 21	5.75 ± 0.5	5.74 ± 0.7	0.98	5.78 ± 0.8	0.90
Day 30	5.52 ± 0.5	6.01 ± 0.6	0.04*	5.8 ± 0.7	0.24

There was a statistically significant difference (*).

Table 3. 24-hour urine pH (Graph 1).

Time	Potassium citrate (Ref) 10 mEq	Potassium citrate (Test) 10 mEq	P between Ref. and Test (10 mEq)	Potassium citrate (Test) 15 mEq	P between Ref. and Test (15 mEq)
Beginning	5.94 ± 0.5	5.88 ± 0.4	0.70	5.79 ± 0.4	0.34
Day 7	5.93 ± 0.6	5.94 ± 0.3	0.96	6.13 ± 0.5	0.32
Day 21	6.10 ± 0.5	5.86 ± 0.9	0.38	5.97 ± 0.8	0.61
Day 30	6.08 ± 0.6	6.16 ± 0.2	0.69	5.83 ± 0.6	0.31

Table 4. Equivalence analysis of the main variable pH of 24-hour urine. Comparison between K CitrateUrocit™ vs K Citrate TEST 10 mEq (logarithmically transformed data to ensure normality).

Time	Minimum IC 95 (%)	Mean (%)	Maximum IC 95 (%)
Beginning	97.85	99.48	101.12
Day 7	98.81	100.23	101.65
Day 21	93.52	97.39	101.27
Day 30	99.86	100.84	101.83

Neither the means nor the CI are below 80% or above 125% for the pH values in 24-h urine, in any of the periods evaluated (Table 5).

There were not statistical differences in other 24-hour urine parameters (Table 6).

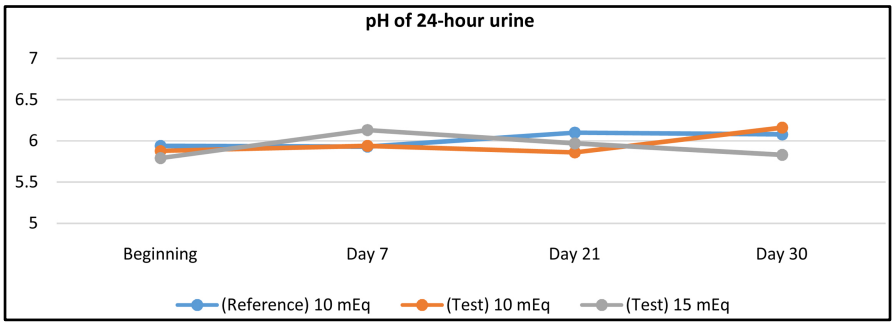
No adverse effects were reported in any group. In laboratory tests, one patient in the Urocit® brand K Citrate group presented elevated transaminases at the end of the study, without other alterations.

3. Discussion

Urolithiasis is common in developed countries, with a prevalence of 10%, and is

Table 5. Equivalence analysis of the main variable pH of 24-hour urine. Comparison between K Citrate Urocit™ vs K Citrate TEST 15 mEq (logarithmically transformed data to ensure normality).

Time	Minimum IC 95 (%)	Mean (%)	Maximum IC 95 (%)
Beginning	96.78	98.54	100.29
Day 7	99.69	101.99	104.30
Day 21	94.71	98.37	102.02
Day 30	90.82	95.83	100.83



Graph 1. Evolution of the means in the pH values of 24-hour urine.

associated with an increased risk of subsequent loss of renal function and cardiovascular disease [16]. The recurrence rate after the first stone episode is up to 40% in the first 5 years and 75% after 20 years [17]. The management of recurrent lithiasis requires knowledge of the risk factors in patients who form stones.

Hypercalciuria and hypocitraturia are the most important risk factors for stone formation, followed by hyperoxaluria and hyperuricosuria [18].

In a retrospective study, 503 patients who received potassium citrate for a median duration of 41 months (range, 6-168). They evaluated the changes in urinary profile: the changes observed werean increased urinary pH (5.90 to 6.46, $p < 0.0001$) and increased urinary citrate (470 to 700 mg daily, $p < 0.0001$) 6 months after the start of therapy.

These patients had a significant decrease in stone formation rate after initiation of potassium citrate from 1.89 to 0.46 stones per year ($p < 0.0001$), a remission rate of 68%, and a decreased 93% in stone formation rate. These changes in profiles kept up to 14 years after starting treatment. The results obtained by this study confirmed the long-term efficacy of potassium citrate therapy in patients with recurrent nephrolithiasis [19].

A review of a database on metabolic renal stone formation in a tertiary care academic hospital was carried out in order to assess the effect of potassium citrate on calcium excretion.

Patients with a history of calcium oxalate nephrolithiasis and hypocitraturia were identified who had received potassium citrate therapy for a minimum of 3 months.

Table 6. Other 24-hour urine parameters.

Time	Potassium citrate (Ref) 10 mEq	Potassium citrate (Test) 10 mEq	P between Ref. and Test (10 mEq)	Potassium citrate (Test) 15 mEq	P between Ref. and Test (15 mEq)
Urinary volume in 24 hours (mL)					
Beginning	2120.67 ± 1022.0	2157.27 ± 1091.9	0.93	2357.50 ± 1125.0	0.54
Day 7	2085.00 ± 1032.1	1904.80 ± 1139.4	0.66	2590.91 ± 1105.7	0.26
Day 21	2207.69 ± 1154.5	1868.21 ± 1043.0	0.43	2665.00 ± 1142.6	0.31
Day 30	1810.0 ± 532.8	1499.00 ± 705.7	0.22	2715.45 ± 1026.0	0.02*
Calcium (50 - 150 mg/24hr)					
Beginning	44.78 ± 22.1	104.61 ± 89.3	0.02*	147.31 ± 99.6	0.00*
Day 7	99.37 ± 190.1	90.86 ± 87.9	0.88	109.83 ± 70.0	0.85
Day 21	80.68 ± 64.7	65.78 ± 53.8	0.52	172.05 ± 118.9	0.02*
Day 30	59.77 ± 45.8	86.57 ± 60.3	0.22	158.16 ± 94.0	0.00*
Sodium (27 - 287 mEq/24hr)					
Beginning	104.2 ± 38.2	99.73 ± 35.2	0.74	90.89 ± 29.7	0.29
Day 7	87.14 ± 23.4	94.08 ± 43.7	0.60	90.45 ± 24.3	0.73
Day 21	119.00 ± 30.4	92.44 ± 35.1	0.04	94.57 ± 20.4	0.02*
Day 30	100.6 ± 21.8	93.61 ± 36.7	0.56	107.09 ± 31.2	0.58
Creatinine(500 - 2000 mg/24hr)					
Beginning	1144.9 ± 1233.2	687.0 ± 308.6	0.18	851.01 ± 304.2	0.15
Day 7	782.01 ± 274.3	708.93 ± 296.2	0.50	783.84 ± 378.1	0.60
Day 21	892.48 ± 418.1	686.69 ± 422.0	0.21	865.16 ± 297.87	0.22
Day 30	723.32 ± 315.2	775.92 ± 473.5	0.74	830.91 ± 211.4	0.71
Phosphorus (380 - 1300 mg/24hr)					
Beginning	1228.00 ± 2020.8	759.53 ± 410.3	0.39	525.00 ± 270.8	0.20
Day 7	642.86 ± 277.9	736.48 ± 400.7	0.47	548.18 ± 506.1	0.59
Day 21	651.67 ± 380.7	613.19 ± 422.7	0.81	500.71 ± 273.5	0.27
Day 30	527.00 ± 247.8	555.79 ± 346.0	0.81	466.36 ± 129.9	0.50
Protein (0 - 300 mg/24hr)					
Beginning	196.27 ± 84.9	216.72 ± 115.0	0.58	153.81 ± 59.4	0.12
Day 7	225.07 ± 125.4	284.15 ± 210.3	0.49	172.27 ± 71.9	0.2
Day 21	239.54 ± 84.3	199.79 ± 89.5	0.25	139.29 ± 49.9	<0.001*
Day 30	223.00 ± 75.1	167.13 ± 67.9	0.07	148.73 ± 38.6	0.01*
Uric acid (250 - 750 mg/24hr)					
Beginning	496.23 ± 154.1			521.72 ± 317.0	0.79
Day 7	461.94 ± 201.4	649.63 ± 572.9	0.30	640.66 ± 652.6	0.40
Day 21	474.19 ± 199.5	573.94 ± 432.4	0.49	447.24 ± 178.4	0.72
Day 30	390.00 ± 168.5	462.09 ± 323.1	0.52	367.44 ± 228.6	0.79

There was a statistically significant difference (*).

The composition of the urine was analyzed, prior to the initiation of potassium citrate therapy and after 3 months of therapy. Patients received 30 - 60 mEq potassium citrate by mouth daily. Inclusion criterion was a change in urine potassium of 20 mEq/day or greater, which suggests compliance with potassium citrate therapy.

Twenty-two patients were evaluated. Mean pre-treatment 24-h urine values were as follows: citrate 280.0 mg/day, potassium 58.7 mEq/day, calcium 216.0 mg/day, pH 5.87. Potassium citrate therapy was associated with statistically significant changes in each of these parameters-citrate increased to 548.4 mg/day ($p < 0.0001$), potassium increased to 94.1 mEq/day ($p < 0.0001$), calcium decreased to 156.5 mg/day ($p = 0.04$), pH increased to 6.47 ($p = 0.001$). Urine sodium excretion was not different pre- and post-therapy (175 mEq/day pre-therapy versus 201 mEq/day post-therapy, p = NS). Urinary calcium excretion decreased by a mean of 60 mg/day on potassium citrate therapy-a nearly 30 % decrease in urine calcium excretion. These data lend support to the hypothesis that alkali therapy reduces urine calcium excretion [20].

In another study evaluating the therapeutic role of potassium citrate in the treatment of renal stones, 56 patients (Mean age = 43.7 ± 10.8) from June 2018 to December 2018 with a total of 86 renal stones enrolled in the study and treated with potassium citrate (10 mEq tablets, three times a day). Moreover, the patients were recommended to reduce sodium intake as well as oxalate-rich foods, have at least 2 liters of water per day and normalize calcium intake. Finally, they were assessed 8 weeks after the treatment initiation, while in those whose stones remained, the assessments were repeated for another 8 weeks. 42 and 25 stones were completely dissolved at the first and second visit, respectively. Compared to the baseline parameters, the mean size of stones in the largest diameter decreased significantly from 5.13 to 1.96 mm and 5.13 to 0.79 mm (p-value < 0.001) at the first and second visit, respectively [21].

Potassium citrate supplementation in patients with a history of kidney stones in Switzerland resulted in a beneficial change in urinary risk profile, particularly increasing anti-lithogenic factors. Fasting glucose, HbA1c, cholesterol levels, and BMI were not affected by potassium citrate therapy after 3 months, suggesting that potassium citrate is safe and not associated with adverse effects, nor metabolic side effects. Finally, 1.25(OH)2 D3 levels were not associated with urinary citrate excretion [22].

In this study, carried out in order to compare the effect of potassium citrate on urinary pH of two new presentations from Laboratorios Leti, S.A.V. against the effect of the innovative drug, we found similar results to previous studies with a slight increase in urinary pH, with no difference between the groups compared

The results of our study show that the variation in urinary pH obtained with the two test products is equivalent to that obtained with the reference product, both in the pH of the simple urine tests, and for the urine samples of 24 hours.

According to all that has been explained, and to the results obtained, no differences are found between the test drugs and the reference drug, and they can be used in the same way for their ability to prevent the formation of kidney stones in people with this predisposition to their formation.

4. Conclusion

Based on the results obtained, and the statistical analyzes performed on the data set collected for the pharmacodynamic equivalence study, it can be concluded that the test formulations K Citrate 10 mEq and K Citrate 7.5 mEq, test products, from Laboratories LETI, S.A.V., administered in doses of 30 mEq daily in patients with a history of kidney stones, are equivalent to the reference product K citrate Urocit® in their effects on urinary pH in 24-hour urine, and in the simple urine test.

Support

Laboratorios Leti, S.A.V.

Conflicts of Interest

Dr. Eloy González and Dr. Tellez Mendez reveal no conflict of interest. Dr. Maria González Yibirín and Dr. David Rincón Matute work at Laboratorios Leti S.A.V.

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