УДК 616.613-003.7
DOI: 10.17816/uroved8218-23

USE OF MINERAL WATER IN REHABILITATION THERAPY OF PATIENTS WITH NEPHROLITHIASIS

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For citation: Nejmark AI, Saldan IP, Davydov AV. Use of mineral water in rehabilitation therapy of patients with nephrolithiasis. *Urologicheskie vedomosti*. 2018;8(2):18-23. doi: 10.17816/uroved8218-23

Received: 23.04.2018 Accepted: 28.05.2018

Background. Study of alternative non-pharmacological methods of rehabilitation therapy is an actual task in the direction of preventive and restorative medicine. An important role in rehabilitation measures in preventing urolithiasis relapse is therapy using balneological therapeutic methods. **The aim** of the study was to perform a clinical and laboratory analysis of the effectiveness of mineral water "Serebrjanniy kluch" (Silver Rill) in rehabilitation therapy for patients with urolithiasis. **Materials and methods.** The study is based on the results of survey data analysis and treatment of 36 patients with urolithiasis. All patients were randomized into two groups: the first (control) group comprised 17 patients who received standard conservative therapy (antispasmodics and analgesics) and fresh drinking water and the second (main) group comprised 19 patients who received standard conservative therapy and mineral drinking water "Serebrjanniy kljuch" at 5 ml/kg of body weight per serving, at 18°C-25°C for 30-40 minutes before meals 4 times a day in an outpatient setting. **Results.** In the second group, self-sustained calculus removal was recorded in 78.9% of cases, and there was an increase in daily diuresis in all patients, a decrease in the excretion of oxalate and uric acid in daily urine by 52.3% and 49.9%, respectively, and decrease and normalization of lactate dehydrogenase, leucine aminopeptidase, and N-acetyl-β-D-glucosaminidase concentrations were 28.3%, 24.5%, and 12.5% ($p < 0.05$), respectively. In addition, the decrease and normalization of the accumulation time indicators were registered 2.7 times ($p < 0.05$), the half-life period was 2.1 times ($p < 0.05$), and the glomerular filtration rate increased by 60.1% ($p < 0.05$) with simultaneous improvement in microcirculation of the kidneys. **Conclusions.** Consuming mineral water "Serebrjanniy kljuch" as a part of rehabilitation therapy of patients with urolithiasis positively influences the clinical course of the disease, helps reduce the excretion of oxalates and uric acid in daily urine, reduces enzymes, and leads to an increase in daily diuresis.

Keywords: nephrolithiasis; mineral water; rehabilitation therapy.

ИСПОЛЬЗОВАНИЕ МИНЕРАЛЬНЫХ ВОД В РЕАБИЛИТАЦИОННОЙ ТЕРАПИИ БОЛЬНЫХ МОЧЕКАМЕННОЙ БОЛЕЗНЬЮ

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Для цитирования: Неймарк А.И., Салдан И.П., Давыдов А.В. Использование минеральных вод в реабилитационной терапии больных мочекаменной болезнью // Урологические ведомости. – 2018. – Т. 8. – № 2. – С. 18–23. doi: 10.17816/uroved8218-23

Дата поступления: 23.04.2018 Статья принята к печати: 28.05.2018

Актуальность. Изучение альтернативных немедикаментозных методов реабилитационной терапии является актуальной задачей профилактического направления восстановительной медицины. Важную роль в реабилитационных мероприятиях по профилактике рецидивов нефролитиаза играет терапия с применением бальнеологических лечебных факторов. **Цель исследования** — клинико-лабораторный анализ эффективности применения слабоминерализованной минеральной воды «Серебряный ключ» в реабилитационной терапии больных мочекаменной болезнью. **Материалы и методы исследования.** Проанализированы данные обследования и лечения 36 больных мочекаменной болезнью. Все пациенты, включенные в исследование, были рандомизированы на две группы: 1-я (контрольная) — 17 человек, которые получали стандартную консервативную терапию (спазмолитики, анальгетики) и питье пресной воды, и 2-я (основная) — 19 человек, получавших стандартную консервативную терапию и питье минеральной воды «Серебряный ключ» по 5 мл/кг массы тела на прием (температура — 18–25 °С), за 30–40 мин до еды 4 раза в день в амбулаторных условиях. **Результаты.** У пациентов 2-й группы самостоятельное отхождение конкремента зарегистрировано в 78,9 % случаев, отмечалось увеличение суточно-

го диуреза у 100 % больных, наблюдалось снижение экскреции оксалатов и мочевой кислоты в суточной моче на 52,3 и 49,9 % соответственно, снижение (и нормализация) концентрации лактатдегидрогеназы, лейцинаминопептидазы и N-ацетил-β-D-глюкозаминидазы на 28,3, 24,5 и 12,5 % ($p < 0,05$) соответственно. Наряду с этим зарегистрированы снижение (и нормализация) показателей времени накопления в 2,7 раза ($p < 0,05$), периода полувыведения — в 2,1 раза ($p < 0,05$) и увеличение скорости клубочковой фильтрации — на 60,1 % ($p < 0,05$) с одновременным улучшением микроциркуляции почек. **Заключение.** Прием минеральной воды «Серебряный ключ» в реабилитационной терапии больных мочекаменной болезнью положительно влияет на клиническое течение заболевания, способствует уменьшению экскреции оксалатов, мочевой кислоты в суточной моче, снижению энзимурии и приводит к увеличению суточного диуреза.

Ключевые слова: мочекаменная болезнь; минеральная вода; реабилитационная терапия.

INTRODUCTION

Urolithiasis is one of the most common and frequent diseases worldwide that develops most often in individuals of working age [1]. Urolithiasis is third among the urological profile diseases, following infections of the urinary tract and diseases of the prostate [2]. Compared with its incidence rate in 2002, the increase in the number of patients with Urolithiasis was 25.1% [3].

The successes achieved in the treatment of Urolithiasis do not contribute to a decrease in the incidence rate, which may be due to the frequent relapses of the disease because of the influence of both exogenous and endogenous factors associated with pathological processes [4, 5].

High occurrence, increasing incidence, frequent relapses, and low efficiency of conservative therapy encourage the search for new methods for its treatment [6, 7].

Intensive development in drug therapy and surgical treatment methods has not solved several issues regarding Urolithiasis prevention and treatment. Moreover, after surgical treatment, relapse occurs in 7–10% of patients within a year, in 35% of patients within 5 years, and in 50% of patients within 10 years after calculus elimination [8].

The study of alternative non-drug methods of rehabilitation therapy is a relevant objective of the preventive direction of restorative medicine [9]. Therapy that uses balneological therapeutic factors plays a very important role in rehabilitation measures to prevent relapses of nephrolithiasis [10, 11].

The therapeutic effect of mineral waters is attributed to their various physical and chemical properties. Their use leads to the restoration of disordered mineral metabolism, thereby increasing the solubility of salts in the urine; water affects the activity of oxidation-reduction enzymes and the content of biologically active substances and contributes to enhancing the diuretic effect, thereby improving renal plasma flow and filtering urine in the renal glomeruli, which in turn leads to a decrease in the relapse of the disease [12, 13].

This study aimed to perform clinical and laboratory analysis of the efficiency of the weakly mineralized water “Serebryany klyuch” (Silver spring) in rehabilitation therapy for patients with Urolithiasis.

MATERIALS AND METHODS OF THE STUDY

In this study, examination and treatment data of 36 patients with Urolithiasis were analyzed. The average age of the patients was 43.7 ± 4.2 (range, 32–52) years. There were 20 (55.6%) men and 16 (44.4%) women.

The duration of nephrolithiasis in the examined patients ranged from 8 months to 7 years. Most (37.8%) of the patients had a disease duration of 1–4 years.

Previously, patients underwent various interventions aimed at the removal of renal and ureteral calculus. In this study, 9 (25%) patients underwent open traditional surgeries, 17 (47.2%) had extracorporeal lithotripsy, 7 (19.5%) underwent contact lithotripsy, and 3 (8.3%) had an independent calculus discharge.

To assess the efficiency of rehabilitation therapy in patients with Urolithiasis, the content of the following urinary excreted enzymes was determined: gamma glutamyltransferase (GGT), lactic dehydrogenase (LDH), alkaline phosphatase (ALP), leucine aminopeptidase (LAP), and N-acetyl-β-D-glucosaminidase (NAG), as well as oxaluria and

excretion of uric acid. Daily diuresis was determined. To assess the functional state of the kidneys, scintigraphy was performed on a Diacam camera using Indium-113 m complex with diethylenetriaminepentaacetic acid. Laser Doppler flowmetry was used to determine kidney microcirculation, which enabled recording of the microcirculation index (MI) as well as the microcirculation efficiency index (MEI), whose value reveals the level of perfusion.

All patients enrolled in the study were randomized into two groups that were comparable in age, sex, clinical manifestations, and disease severity based on the typological selection method: group 1 (control), which included 17 patients who received standard conservative therapy (antispasmodics and analgesics) and fresh water to drink, and group 2 (study), which included 19 patients who received standard conservative therapy and the mineral water "Serebryany klyuch" at a dose of 5 ml/kg of body weight per intake (temperature, 18–25°C) at 30–40 min before meals four times a day in the outpatient setting.

According to the chemical composition, "Serebryany klyuch" is weakly mineralized hydrocarbonate magnesium-calcium water with weak alkaline reaction.

RESULTS AND DISCUSSION

The primary symptoms of the disease in the patients examined before treatment were dull, dragging pain in the lumbar region in 34 (94.4%) patients, dysuric manifestations in 28 (77.8%), frequent urination in 32 (88.9%), and nausea and vomiting in 14 (38.9%) patients. In group 1, which received spasmolytic therapy with a regular water consumption schedule, following treatment for 14 days, pain in the lumbar region persisted in 11 (64.7%) patients, dysuria persisted in 9 (52.9%), and 3 (17.6%) patients had an independent discharge of microliths. In group 2, with a complex therapy supplemented with the mineral water "Serebryany klyuch," more frequent calculus discharge was recorded in 15 (78.9%) patients, which was accompanied by a decrease in the incidence of pain syndrome in 17 (89.5%) patients, dysuric manifestations in 16 (84.2%) patients, and vegetative symptoms in all patients.

Before the treatment, changes in urine, characterized by proteinuria and erythrocyturia, were recorded and compared between the groups, of which 67% of patients had oxalaturia, 18% had uraturia, and 15% had phosphaturia. In addition, a statistically significant increase in oxalate and uric acid excretion in daily urine and a decrease in daily diuresis were observed (Table 1).

In group 1, a statistically significant increase in daily diuresis was observed after treatment in up to 1232.0 ± 32.1 ml ($p < 0.001$); in group 2, along with an increase in daily diuresis to 1424.0 ± 49.6 ml ($p < 0.001$), a decrease in oxalate and uric acid excretion in daily urine was recorded at 52.3% and 49.9%, respectively ($p < 0.05$). The decrease in oxalate and uric acid excretion in daily urine was due to the presence of magnesium ions in the mineral water, which have a positive effect on hypercalciuria and hyperoxaluria reduction, and calcium ions, which increase the solubility of uric acid in urine [14].

Table 1

Dynamics of 24-h excretion of uric acid, oxalates, and daily diuresis in patients with nephrolithiasis ($M \pm m$)

Indices	Control ($n = 16$)	Group 1 ($n = 17$)		Group 2 ($n = 19$)	
		Before treatment	After treatment	Before treatment	After treatment
Uric acid, mmol/day	3.8 ± 0.24	7.89 ± 0.45 $p_1 = 0.001$	5.73 ± 0.54 $p_1 < 0.001$	7.73 ± 0.35 $p_1 < 0.001$	3.87 ± 0.21 $p_2 = 0.005$
Oxalates, mmol/day	0.19 ± 0.02	0.43 ± 0.04 $p_1 = 0.001$	0.38 ± 0.03 $p_1 = 0.015$	0.44 ± 0.03 $p_1 < 0.001$	0.21 ± 0.07 $p_2 = 0.022$
Daily diuresis, ml	1369.0 ± 43.4	810.0 ± 36.6 $p_1 < 0.001$	1232.0 ± 32.1 $p_2 < 0.001$	837.0 ± 21.7 $p_1 < 0.001$	1424.0 ± 49.6 $p_2 < 0.001$

Note: p_1, significant differences with control values; p_2, significant differences before and after treatment

On assessing the enzymuria indices, an increase in the activity of excreted enzymes was found in both groups (Table 2).

After treatment in group 1, despite a statistically significant decrease in the activity of all enzymes, none of the indices attained the level of the control values. Group 2 had a statistically significant decrease (and normalization) in LDH, LAP, and NAG concentrations by 28.3%, 24.5%, and 12.5% (p <0.05), respectively. Significant dynamics in the change in GGT and ALP levels was not recorded; the indices remained above the control values. This effect of the mineral water "Serebryany klyuch" is attributed to the fact that in case of a decrease in the oxalate-calcium crystalluria, the damaged epithelial cells of the proximal part of the nephron are restored [15].

Based on the renal scintigraphy results, before the treatment, an increase in the accumulation time and half-life of the radiopharmaceutical agent and decrease in the glomerular filtration rate (GFR) was recorded in both groups compared with the control indices (Table 3).

In group 1, after the rehabilitation therapy, there was a tendency of normalization of the parameters

Table 2

Dynamics of indices of enzymuria in patients with nephrolithiasis ($M \pm m$)

Indices	Control (n = 16)	Group 1 (n = 17)		Group 2 (n = 19)	
		Before treatment	After treatment	Before treatment	After treatment
GGT, U/L	5.34 ± 0.28	7.83 ± 0.24 p_1 = 0.001	7.67 ± 0.28 p_1 = 0.006	7.52 ± 0.29 p_1 < 0.001	6.12 ± 0.21 p_1 = 0.013 p_2 = 0.025
ALP, U/L	9.23 ± 0.34	12.67 ± 0.34 p_1 = 0.002	12.45 ± 0.44 p_1 = 0.002	12.34 ± 0.52 p_1 = 0.001	12.23 ± 0.34 p_1 = 0.001
LDH, U/L	6.15 ± 0.21	9.23 ± 0.35 p_1 = 0.001	8.46 ± 0.34 p_1 = 0.020	9.74 ± 0.19 p_1 = 0.001	6.98 ± 0.13 p_2 = 0.005
LAP, U/L	8.22 ± 0.23	11.54 ± 0.76 p_1 = 0.016	10.38 ± 0.43 p_1 = 0.011	10.92 ± 0.35 p_1 = 0.002	8.24 ± 0.18 p_2 = 0.033
NAG, U/mmol creatinine	20.45 ± 0.37	24.87 ± 0.46 p_1 = 0.004	23.017 ± 0.39 p_1 = 0.013	24.15 ± 0.32 p_1 = 0.001	21.12 ± 0.18 p_2 = 0.011

Note: ALP, alkaline phosphatase; GGT, gamma glutamyltransferase; LAP, leucine aminopeptidase; LDH, lactic dehydrogenase; NAG, N-acetyl-β-D-glucosaminidase; p_1, significant differences with control values; p_2, significant differences before and after treatment

Table 3

Dynamics of renal functional status in patients with nephrolithiasis ($M \pm m$)

Indices	Control (n = 16)	Group 1 (n = 17)		Group 2 (n = 19)	
		Before treatment	After treatment	Before treatment	After treatment
T_{max} of accumulation, min	4.12 ± 0.32	13.52 ± 1.32 p_1 < 0.001	9.73 ± 1.12 p_1 < 0.001 p_2 < 0.014	13.67 ± 1.22 p_1 < 0.001	5.07 ± 0.43 p_2 < 0.001
T elimination half-life, min	10.54 ± 0.63	23.17 ± 2.03 p_1 < 0.001	17.45 ± 1.65 p_1 < 0.001 p_2 < 0.001	22.97 ± 1.23 p_1 < 0.001	11.13 ± 0.55 p_2 < 0.001
GFR, ml/min	42.80 ± 3.17	26.98 ± 2.11 p_1 < 0.001	34.18 ± 2.27 p_1 < 0.036 p_2 < 0.018	26.45 ± 1.98 p_1 < 0.001	42.37 ± 1.96 p_2 < 0.001

Note: GFR, glomerular filtration rate; p_1, significant differences with control values; p_2, significant differences before and after treatment

Table 4

Dynamics of basal blood flow at the renal projection point in patients (M ± m)

Indices	Control (n = 16)	Group 1 (n = 17)		Group 2 (n = 19)	
		Before treatment	After treatment	Before treatment	After treatment
IM, PU	20.84 ± 1.12	9.67 ± 0.98 $p_1 < 0.001$	11.78 ± 0.45 $p_1 < 0.001$ $p_2 < 0.001$	9.84 ± 0.39 $p_1 < 0.001$	19.86 ± 0.48 $p_2 < 0.001$
MEI, %	0.89 ± 0.03	0.31 ± 0.02 $p_1 < 0.001$	0.59 ± 0.07 $p_1 < 0.045$ $p_2 < 0.032$	0.39 ± 0.06 $p_1 < 0.020$	0.87 ± 0.02 $p_2 < 0.001$

Note: IM, indicators of microcirculation; MEI, microcirculation efficiency index; PU, perfusion unit; p_1, significant differences with control values; p_2, significant differences before and after treatment

investigated, but they were statistically significantly different from the control values. In group 2 patients, a 2.7-fold decrease (and normalization) in accumulation time indicators ($p < 0.05$), a 2.1-fold decrease in half-life ($p < 0.05$), and a 60.1% increase in GFR ($p < 0.05$) were recorded. This is attributable to the diuretic and osmotic effects of mineral salts and improvement in filtration and secretion processes in the nephron.

Analysis of microcirculation of the kidneys revealed changes in basal blood flow, which was manifested in a decrease in MI and MEI (Table 4).

Following rehabilitation therapy, group 1 patients had no statistically significant changes in the normalization of the values investigated. When group 2 patients consumed the mineral water "Serebryany klyuch," an increase (and normalization) in MI, from 9.84 ± 0.39 to 19.86 ± 0.48 perfusion units (PU) ($p_1 < 0.001$), and MEI, from 0.39 ± 0.06 to 0.87 ± 0.02% ($p_1 < 0.001$), was recorded. This effect is possibly because of a decrease in interstitial edema, normalization of vascular tone, and improvement of the rheological properties of blood [16].

CONCLUSIONS

Inclusion of "Serebryany klyuch" in the rehabilitation therapy of patients with Urolithiasis has a positive effect on the clinical course of the disease and frequency of calculus discharge, helps reduce oxalate and uric acid excretion in daily urine, reduces enzymuria, and leads to an increase in daily diuresis. When consuming mineral water, the kidney GFR increases, and the kidney microcirculation normalizes.

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