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Research Article

Bioregulatory therapy for chronic abacterial prostatitis

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BACKGROUND: Chronic abacterial prostatitis/chronic pelvic pain syndrome (CAP/CPPS) is the most common form of chronic prostatitis.

AIM: The aim of the study was to evaluate the effectiveness and tolerability of complex therapy in patients with CAP/CPPS using the bioregulatory peptide drug Uroprost-D.

MATERIALS AND METHODS: The study included 47 men aged 23 to 54 years (mean 38.1 ± 7.2 years) with CAP/CPPS (category III according to the NYHA classification, 1995). Patients of the 1st group (*n* = 24) were prescribed alpha-blocker tamsulosin 0.4 mg for 30 days and rectal suppositories Uroprost-D one per day for 15 days. Patients of the 2nd group (*n* = 23) were also prescribed tamsulosin 0.4 mg per day for 30 days and rectal suppositories indomethacin 100 mg, one per day for 15 days. The dynamics of clinical parameters was assessed on the 15, 30 and 60th day from the start of the study.

RESULTS: By the 15th day of the study, there was a significant positive dynamics of symptoms in patients of both groups. By the 30th day of the study in patients of the 1st group the treatment effect persisted, while in patients of the 2nd group pain increased, which was expressed in an increase in the scores for the "Pain" domains and the total score of the NIH-CPSI questionnaire. This trend is even more pronounced by the 60th day of observation, when a significant difference was found both in the total score of the NIH-CPSI questionnaire and separately in the domains "Pain", "Dysuria" and "Quality of life". During the study, there were no statistically significant changes in the maximum urine flow rate, prostate volume and residual urine volume. Tolerability of treatment was satisfactory, the frequency of negative manifestations was slightly higher in patients of the 2nd group.

CONCLUSIONS: The use of the bioregulatory peptide drug Uroprost-D in the complex therapy of patients with CAP was accompanied by a decrease in the severity of pain syndrome and dysuria. The appointment of Uroprost-D seems to be a pathogenetically justified alternative to the use of NSAIDs in this category of patients.

Keywords: chronic abacterial prostatitis; chronic pelvic pain syndrome; prostatic peptides; Uroprost-D.

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Научная статья

Биорегулирующая терапия больных хроническим абактериальным простатитом

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Актуальность. Хронический абактериальный простатит / синдром хронической тазовой боли — наиболее частая форма хронического простатита.

Цель исследования — оценка эффективности и переносимости комплексной терапии больных хроническим абактериальным простатитом / синдромом хронической тазовой боли с использованием биорегуляторного пептидного препарата Уропрост-Д.

Материалы и методы. Под наблюдением находились 47 мужчин в возрасте от 23 до 54 лет (в среднем 38,1 ± 7,2 года) с хроническим абактериальным простатитом / синдромом хронической тазовой боли (категория III по классификации NYHA, 1995). Пациентам 1-й группы (n = 24) назначали альфа-адреноблокатор тамсулозин по 0,4 мг в течение 30 дней и ректальные суппозитории Уропрост-Д по одному в сутки в течение 15 сут. Пациентам 2-й группы (n = 23) также назначали тамсулозин по 0,4 мг в сутки в течение 30 дней и ректальные суппозитории Индометацин 100 мг по одному в сутки в течение 15 сут. Динамику клинических показателей оценивали на 15, 30 и 60-е сутки от начала исследования.

Результаты. К 15-му дню исследования отмечена значимая положительная динамика симптоматики у пациентов обеих групп. К 30-му дню у пациентов 1-й группы эффект лечения сохранялся, в то время как во 2-й группе отмечено усиление болей, что выражалось в увеличении баллов по доменам «Боль» и суммарного балла по опроснику NIH-CPSI. Данная тенденция еще более стала выражена к 60-му дню наблюдения. Достоверное различие отмечено как по суммарному баллу по опроснику NIH-CPSI, так и отдельно по доменам «Боль», «Дизурия» и «Качество жизни». В процессе исследования не отмечено статистически значимых изменений максимальной скорости потока мочи, объема предстательной железы и объема остаточной мочи. Переносимость лечения была удовлетворительной, частота негативных проявлений несколько выше у пациентов 2-й группы.

Выводы. Применение биорегуляторного пептидного препарата Уропрост-Д в комплексной терапии больных хроническим абактериальным простатитом сопровождалось снижением выраженности болевого синдрома и дизурии. Назначение Уропроста-Д представляется патогенетически обоснованной альтернативой использованию нестероидных противовоспалительных средств у данной категории больных.

Ключевые слова: хронический абактериальный простатит; синдром хронических тазовых болей; простатические пептиды; Уропрост-Д.

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ЭКО•ВЕКТОР

BACKGROUND

Chronic prostatitis is one of the most common diseases in men. The risk of prostatitis increases with age; for example, in men aged 50–59 years, it is detected 3.1 times more often than in men aged 20–39 years [1]. The most common form of chronic prostatitis is chronic abacterial prostatitis/chronic pelvic pain syndrome (CAP/CPPS, category III according to the prostatitis classification of the US National Institute of Health, NYHA, 1995), which accounts for 90% of all prostatitis forms. CAP has two forms, namely, inflammatory (IIIA) and non-inflammatory (IIIB, CPPS) CAP [2].

The main clinical manifestations of CAP/CPPS are pain, urination disorders and sexual disorders, which significantly worsen the quality of life of patients. CAP/CPPS is characterised by a relapsing course, when periods of disease exacerbation are replaced by periods of relative well-being. The causes of CAP/CPPS are not completely clear; however, most researchers recognise haemodynamic disorders in the prostate gland as the main factor in the disease pathogenesis, which occurs because of blood stagnation in the veins of the small pelvis [3–5]. To date, many therapeutic approaches have been proposed for the treatment of CAP/CPPS, many of which are becoming the subject of discussion [6–10]. Moreover, the necessity of complex disease treatment is recognised because monotherapy with any drug is most often ineffective [6]. The treatment of patients with CAP/CPPS, manifested by pain and urination disorders, must include alpha-adrenoblockers and non-steroidal anti-inflammatory drugs (NSAIDs), as well as a course of antibiotic therapy with broad-spectrum drugs because of the high probability of a false-negative microbiological test result of the third-catch urine sample and prostate secretion [6, 11]. Furthermore, the efficiency of existing methods of CAP/CPPS treatment is often insufficient; therefore, the search for new treatment approaches is very relevant [12]. The therapy in patients with CAP/CPPS is unsuccessful because of sclerotic changes in the prostate gland, which significantly impair the penetration of drugs into it [13]. Thus, when planning therapeutic measures in patients with CAP/CPPS, the prescription of drugs that improve haemodynamics in the pelvis and the penetration of drugs into the prostatic tissue must be considered [6, 9, 10].

One of the promising methods for the treatment of patients with CAP/CPPS is the administration of prostatic bioregulatory peptides. This group of drugs has pronounced tissue specificity, that is, tropism for the organ from which they are isolated [14]. Prostatic peptides, which possessed pronounced systemic effects, have the greatest effect on their target organ, i.e., prostate gland. Drugs based on prostatic regulatory peptides have high biological activity. They have anti-inflammatory and immunotropic effects, ability to improve the rheological properties of blood and microcirculation in the prostate tissue and direct myotropic effect on the detrusor [15–17]. To date, significant experience has been gained in the use of prostatic peptides in the treatment of patients with urological problems, including patients with chronic prostatitis [18–24]. In addition, relatively few studies have examined the efficiency of the combination therapy of CAP/CPPS using prostatic peptides. Thus, in the treatment of patients with CAP/CPPS, studying the efficacy and tolerability of a combination of the alpha-adrenoblocker tamsulosin and rectal suppository Uroprost-D, which includes a bioregulatory peptide from the prostate gland and dimethyl sulfoxide with penetrant properties, appears very relevant.

This study aimed to comparatively assess the efficacy and tolerability of combination therapy in patients with CAP/CPPS, manifested by pain syndrome and urination disorders, using the bioregulatory peptide drug Uroprost-D (rectal suppositories).

MATERIALS AND METHODS

The study included 47 men aged 23–54 (mean 38.1 ± 7.2) years with CAP/CPPS (category III according to the NYHA classification, 1995), clinically manifested as pain syndrome and urination disorders. CAP/CPPS was diagnosed based on the criteria specified in the Russian and international clinical guidelines (negative results of bacteriological examination of the third-catch urine sample after prostate massage and prostate secretion). Chronic non-bacterial inflammatory prostatitis (subcategory IIIA according to the NYHA classification, 1995) was diagnosed in 28 (59.6%) patients, and 19 (40.4%) patients were diagnosed with non-inflammatory prostatitis/CPPS (subcategory IIIB). CAP subcategories IIIA and IIIB were diagnosed based on the results of the analysis of the third-catch urine sample after prostate massage and prostate secretion. When ⩾10 leukocytes were detected in high-resolution microscopy (×400), chronic inflammatory abacterial prostatitis was diagnosed (subcategory IIIA). The disease duration varied from 1 to 10 years (average, 4.1 ± 2.1 years). All patients received antibiotic therapy for at least 4 weeks 1–3 months before inclusion in the study, in accordance with the Russian clinical guidelines, which had no significant effect.

The inclusion criteria for the study were as follows: age >18 years; presence of CAP/CPPS (category III), according to the National Institute of Health Chronic Prostatitis Symptom Index (NIH-CPSI) scale; severity of pain in item 4 of ⩾4 points; urination disorders in items 5 and 6 (total) of ⩾4 points; absence of significant infravesical obstruction; duration of clinical manifestations of CAP/CPPS for at least 1 year; negative result of bacteriological examination of the third-catch urine sample after

prostate massage and prostate secretion for microflora (titre <10^3 CFU in 1 mL); negative result of the analysis for chlamydia, mycoplasma, ureaplasma and gardnerella in the prostate gland secretion and scraping from the urethra by polymerase chain reaction; antibacterial therapy lasting at least 4 weeks with drugs specified in the clinical guidelines for the treatment of chronic prostatitis 1–3 months prior to inclusion in studies, without clinical effect; and signed informed consent to participate in the study.

The exclusion criteria were as follows: acute or bacterial chronic prostatitis; intake during the study period of any drugs that affect urinary tract and prostate gland function, except for those prescribed within the study; individual intolerance or contraindications to the use of Uraprost-D, indomethacin and tamsulosin; prostate-specific antigen level in the blood serum of more than 4 ng/mL; oncological diseases of the pelvic organs at present or in history; history surgical interventions on the prostate gland and lower urinary tract; neurogenic dysfunction of the lower urinary tract; diseases that can cause pain in the pelvic area and/or urinary disorders (painful bladder syndrome/interstitial cystitis, urethral stricture, malformations of the lower urinary tract, bladder stones and lower urinary tract malformations).

At the screening stage, all patients underwent a general urological examination, which included an assessment of case history and complaints; physical examination; laboratory tests, including bacteriological and general clinical examination of the third-catch sample of morning urine and prostate secretion and a polymerase chain reaction study of urethra scrapings and prostate gland secretion for chlamydia, mycoplasma, ureaplasma and gardnerella; ultrasonography of the bladder and prostate gland with the determination of the residual urine volume; uroflowmetry; and assessment of symptom severity using the NIH-CPSI questionnaire, International Prostate Symptom Score (IPSS) and International Index of Erectile Function (IIEF-5).

At the initial examination, all patients complained of pain (in nearly all cases in the perineal region and less often in the testicles, glans penis and area above the womb) and urination disorders. The total score on the NIH-CPSI scale was 20.9 ± 4.1 (15–35 points), the average score for the 'Pain' domain was 8.5 ± 2.5 (6–15), 6.4 ± 1.4 (4 to 10) for the 'Dysuria' domain and 5.9 ± 2.6 (2–11) for the 'Quality of life' domain. The total score for the 'Pain' and 'Dysuria' domains was 15.0 ± 2.6. The severity of CAP/CPPS symptoms in 45 (95.7%) patients corresponded to a moderate degree (10–18 points in the 'Pain' and 'Dysuria' domains); in 2 (4.3%) patients, it corresponded to a severe degree (>19 points in the 'Pain' and 'Dysuria' domains). The mean score on the IPSS scale was 8.6 ± 3.0 (5–15) points, whereas the score corresponded to mild symptoms (0–7 points) in 18 (38.3%) patients and moderate symptoms (8–19 points) in 29 (61.7%). In the assessment of the degree of erectile dysfunction according to the IIEF-5 scale, erectile dysfunction was noted in 19 (40.4%) of 47 patients. Erectile dysfunction was mild in 15 (31.9%) men and moderate in 4 (8.5%). The average prostate gland volume was 21.9 ± 4.6 (12–29) cm^3, and the residual urine volume was 19.9 ± 13.1 (0–45) mL. In 19 (40.4%) patients, the maximum volumetric urine flow rate (Q_{max}) decreased to <15 mL/s. The average Q_{max} value was 17.6 ± 4.4 mL/s, which ranged from 13 to 27 mL/s.

By random sampling, all patients were distributed into two groups: group 1 (main) included 25 patients, and group 2 included 23 patients. Both groups were comparable in age, basic anamnesis and clinical parameters (Table 1).

Group 1 (main) received the alpha-adrenoblocker tamsulosin 0.4 mg once a day for 30 days and the rectal suppository Uroprost-D (once a day) for 15 days, with a total of 15 suppositories per course. Group 2 (control) received the alpha-adrenoblocker tamsulosin 0.4 mg once a day for 30 days and rectal suppository indomethacin (100 mg, once a day) for 15 days, with a total of 15 suppositories per course. Both groups were recommended to use rectal suppositories at night before bed after defecation. During the follow-up period, patients were recommended to adhere to a certain lifestyle, which included avoidance of spicy and excessively salty food and alcohol.

The dynamics of clinical parameters were assessed on days 15, 30 and 60 from the start of the study. The treatment efficiency was assessed by changes in the total score and indicators of the 'Pain', 'Dysuria' and 'Quality of life' domains of the NIH-CPSI scale, total points according to the IPSS questionnaire, and total score according to the IIEF-5 questionnaire. During these periods, the leukocyte counts in the third-catch urine sample obtained from patients after prostate massage was determined, and uroflowmetry and ultrasound examination of the prostate gland were performed to determine the residual urine volume. The total follow-up duration for one patient was 2 months.

Statistical analysis of data was performed with Statistica 10 En (StatSoft, Inc.) using the *t*-test, Pearson's χ^2 test and Fisher's exact method (*F*-test). Differences were considered significant at $p < 0.05$. Average values of indicators are presented with mean square deviation ($M \pm \sigma$)

RESULTS

When analysing the results of the patient survey using the NIH-CPSI questionnaire, a significant positive dynamic of symptoms was noted by day 15 in both groups (Table 2).

Table 1. Characteristics of patients with chronic abacterial prostatitis / chronic pelvic pain syndrome of the main and control groups (n = 47)

Таблица 1. Характеристика больных хроническим абактериальным простатитом / синдромом хронической тазовой боли основной и контрольной групп (n = 47)

Parameter	Group 1 (main) (n = 24)	Group 2 (control) (n = 23)
Age, years	38.6 ± 8.5 (23–54)	37.6 ± 9.0 (25–51)
Disease duration, years	4.1 ± 2.0 (1–9)	4.1 ± 2.2 (1–10)
Subcategories: IIIA, chronic inflammatory non-bacterial prostatitis, n	14 (58.3%)	14 (60.9%)
IIIB, non-inflammatory prostatitis — chronic pelvic pain syndrome, n	10 (41.7%)	9 (39.1%)
Total NIH-CPSI scores	20.8 ± 3.4 (15–27)	21.0 ± 4.9 (15–35)
NIH-CPSI 'Pain' domain score	8.5 ± 2.5 (6–15)	8.7 ± 2.6 (6–16)
NIH-CPSI 'Dysuria' domain score	6.5 ± 1.3 (4–9)	6.3 ± 1.5 (4–10)
NIH-CPSI score on the 'Pain' and 'Dysuria' domains	14.9 ± 2.5 (11–23)	15.0 ± 2.8 (10–24)
NIH-CPSI score on the 'Quality of life' domain	5.8 ± 2.5 (2–11)	6.0 ± 2.7 (2–11)
Score on the IPSS questionnaire	8.5 ± 4.1 (6–15)	8.8 ± 3.8 (5–15)
Q_{max}, mL/s	17.6 ± 4.1 (13–26)	17.9 ± 4.7 (13–27)
Residual urine volume, mL	21.5 ± 13.9 (0–45)	18.0 ± 12.5 (0–43)
Prostate volume, cm^3	22.3 ± 4.2 (15–29)	21.4 ± 4.3 (14–28)

Note. For all pairs of signs $p > 0,1$. Q_{max} — urine flow rate.

Table 2. Dynamics of NIH-CPSI scores in patients of groups 1 and 2 during treatment and observation, scores ($M \pm \sigma$)

Таблица 2. Динамика показателей шкалы NIH-CPSI у пациентов 1-й и 2-й групп в процессе лечения и наблюдения, баллы ($M \pm \sigma$)

Parameter	Group	Before treatment	Day 15	Day 30	Day 60
Total score	1 (n = 24)	20.8 ± 3.4	10.6 ± 2.3*	9.0 ± 2.2*.**	9.2 ± 2.2*. **
	2 (n = 23)	21.0 ± 4.9	10.4 ± 3.0*	12.9 ± 2.3*	19.3 ± 3.5
Domain 'Pain'	1 (n = 24)	8.5 ± 2.5	5.8 ± 2.1*	5.4 ± 1.7*.**	5.3 ± 1.8*. **
	2 (n = 23)	8.7 ± 2.6	5.3 ± 1.7*	7.0 ± 2.1*	8.4 ± 2.6
VAS for pain (NIH-CPSI item 4)	1 (n = 24)	4.6 ± 1.2	3.4 ± 1.6*	3.4 ± 1.9*	3.4 ± 1.7*. **
	2 (n = 23)	4.8 ± 1.2	3.0 ± 1.9*	4.0 ± 1.4	4.5 ± 1.3
Domain 'Dysuria'	1 (n = 24)	6.5 ± 1.3	1.8 ± 1.4*	1.3 ± 1.2*	1.5 ± 1.6*. **
	2 (n = 23)	6.3 ± 1.5	1.7 ± 1.2*	1.4 ± 1.1*	5.6 ± 1.6
Total 'Pain' and 'Dysuria'	1 (n = 24)	14.9 ± 2.5	7.3 ± 1.9*	6.6 ± 1.8*	6.9 ± 1.8*. **
	2 (n = 23)	15.0 ± 2.8	7.2 ± 2.1*	8.0 ± 2.0*	13.9 ± 3.1
Domain 'Quality of life'	1 (n = 24)	5.8 ± 2.5	3.4 ± 1.8*	2.4 ± 1.1*.**	2.2 ± 1.2*. **
	2 (n = 23)	6.0 ± 2.7	3.2 ± 1.5*	4.4 ± 1.6*	5.4 ± 2.2

* Difference is statistically significant compared with the indicator before treatment ($p < 0.05$). ** Difference is statistically significant compared with the indicator in group 2 ($p < 0.05$).

Statistically significant differences in comparison with baseline values in groups 1 and 2 were registered in the total score of the questionnaire, domains 'Pain', 'Dysuria' and 'Quality of life' and a sum of the scores in the domains 'Pain' and 'Dysuria'. By day 30, similar dynamics were also noted. However, during this period, in group 2 patients who received rectal suppositories with indomethacin, an increase in pain was noted, which was expressed as an increase in score for the 'Pain' domain, item 4 of the NIH-CPSI questionnaire, visual analogue scale (VAS) of pain, total score for domains 'Pain' and 'Dysuria' and total score of the NIH-CPSI questionnaire. By day 30 of follow-up, i.e., 15 days after the end of treatment with Uroprost-D (group 1) and indomethacin (group 2), group 1 showed statistically significant differences with group 2 in terms of the NIH-CPSI total scores,

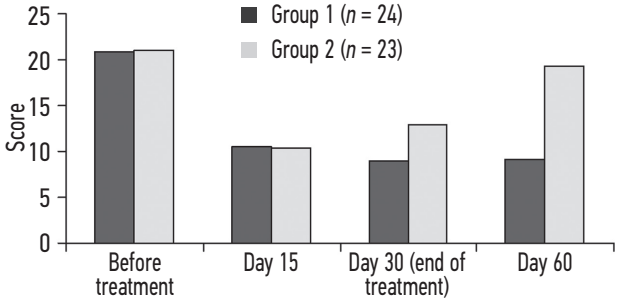

Fig. 1. Dynamics of the total score of the NIH-CPSI scale in patients of the 1st and 2nd groups (n = 47). The difference in patients of the two groups by the 30th and 60th days of observation was statistically significant

Рис. 1. Динамика суммарного балла шкалы NIH-CPSI у пациентов 1-й и 2-й групп (n = 47). Различие у пациентов двух групп к 30-му и 60-му дням наблюдения статистически достоверно

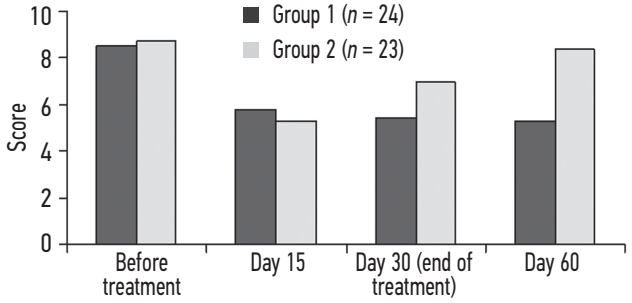

Fig. 2. Dynamics of the total score for the "Pain" domain of the NIH-CPSI scale in patients of the 1st and 2nd groups (n = 47). The difference in patients of the two groups by the 30th and 60th days of observation was statistically significant

Рис. 2. Динамика суммарного балла по домену «Боль» шкалы NIH-CPSI у пациентов 1-й и 2-й групп (n = 47). Различие у пациентов двух групп к 30-му и 60-му дням наблюдения статистически достоверно

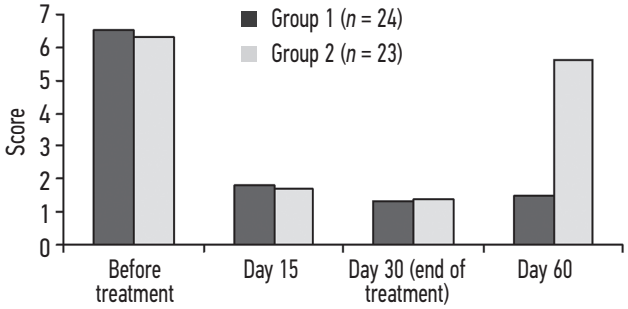

Fig. 3. Dynamics of the total score for the "Dysuria" domain of the NIH-CPSI scale in patients of the 1st and 2nd groups (n = 47). The difference in patients of the two groups by the 60th day of observation was statistically significant

Рис. 3. Динамика суммарного балла по домену «Дизурия» шкалы NIH-CPSI у пациентов 1-й и 2-й групп (n = 47). Различие у пациентов двух групп к 60-му дню наблюдения статистически достоверно

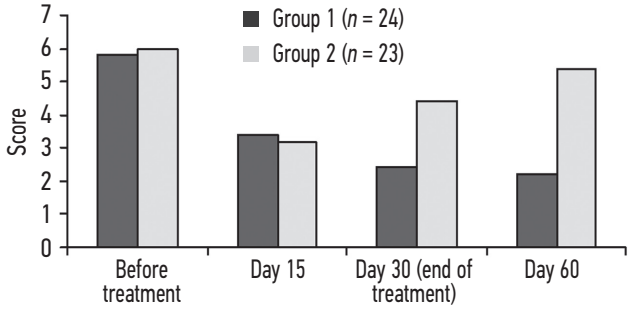

Fig. 4. Dynamics of the total score for the "Quality of Life" domain of the NIH-CPSI scale in patients of the 1st and 2nd groups (n = 47). The difference in patients of the two groups by the 30th and 60th days of observation was statistically significant

Рис. 4. Динамика суммарного балла по домену «Качество жизни» шкалы NIH-CPSI у пациентов 1-й и 2-й групп (n = 47). Различие у пациентов двух групп к 30-му и 60-му дням наблюдения статистически достоверно

total scores of 'Pain' and 'Quality of life' domains and NIH-CPSI item 4 (VAS of pain). This indicated the resumption of pain in group 2, whereas the effect was maintained in group 1. This trend was even more pronounced by day 60 of follow-up (day 30 after the end of tamsulosin intake). A significant difference was noted in the total score of the NIH-CPSI questionnaire and separately in the domains 'Pain', 'Dysuria' and 'Quality of life' (Figs. 1–4).

Analysis of the IPSS questionnaire responses showed a significant decrease in the total score by day 15 of treatment in groups 1 and 2. When questioned on day 30 of treatment and day 60 of follow-up (30 days after the end of treatment), in both groups, the total scores according to the IPSS questionnaire were also significantly lower than the baseline values. Moreover, in both groups, by day 60 of follow-up, a trend was found toward an increase in the total IPSS scores, but it was more pronounced in group 2 (Table 3, Fig. 5).

During the study, no statistically significant changes were found in the maximum urine flow rate (Q_{max}), prostate volume and residual urine volume. The results of the analysis of the third-catch urine sample obtained after a prostate massage showed a decrease in the incidence of leukocyturia in both groups 1 and 2. An increased white blood cell count in urine sample 3 indicates CAP subcategory IIIA (chronic inflammatory non-bacterial prostatitis). Before treatment, this form of chronic prostatitis was diagnosed in 14 (58.3%) patients of group 1 and 14 (60.9%) of group 2, and by day 30, the leukocyte counts in the third-catch urine sample increased in 9 (37.5%) patients of group 1 and 8 (34.8%) of group 2. During the examination on day 60 of treatment, the inflammatory form of CAP was confirmed in 10 (41.7%) patients of group 1 and 11 (47.8%) of group 2. The difference in the frequency of detection of CAP subcategory IIIA in groups 1 and 2 by days 30 and 60 of follow-up was not statistically significant ($\chi^2 = 0.038$, $p > 0.1$ and $\chi^2 = 0.18$, $p > 0.1$, respectively).

Table 3. Dynamics of clinical parameters in patients of groups 1 and 2 during treatment and observation ($M \pm \sigma$)
Таблица 3. Динамика клинических показателей у пациентов 1-й и 2-й групп в процессе лечения и наблюдения ($M \pm \sigma$)

Parameter	Group	Before treatment	Day 15	Day 30	Day 60
IPSS total score	1 (n = 24)	8.5 ± 2.0	2.7 ± 2.3*	1.5 ± 1.6*	3.1 ± 2.3*
	2 (n = 23)	8.8 ± 3.8	2.7 ± 2.2*	1.7 ± 1.8*	5.1 ± 2.5*
Q_{max}, mL/s	1 (n = 24)	17.5 ± 4.4	19.6 ± 4.6	20.1 ± 4.5	19.8 ± 4.3
	2 (n = 23)	17.9 ± 4.6	19.2 ± 4.7	20.3 ± 4.3	18.2 ± 4.3
Prostate volume, cm^3	1 (n = 24)	22.3 ± 4.2	–	21.9 ± 4.3	20.2 ± 4.2
	2 (n = 23)	21.4 ± 4.2	–	19.9 ± 4.2	20.2 ± 4.0
Residual urine volume, mL	1 (n = 24)	21.5 ± 12.9	–	17.4 ± 12.7	19.7 ± 13.2
	2 (n = 23)	18.0 ± 12.5	–	20.1 ± 12.6	21.7 ± 10.5

* Difference is statistically significant compared with the indicator before treatment ($p < 0.05$). ** Difference is statistically significant compared with the indicator in group 2 ($p < 0.05$). *Note*. Q_{max} — urine flow rate.

All study patients were surveyed using the IIEF-5 questionnaire to assess their erectile function. A score of >20 points indicated normal erectile function; 16–20, mild; and 11–15, moderate. Moreover, 19 (40.4%) of the 47 patients with CAP before the start of treatment had an IIEF-5 score of ⩽20, which indicated erectile dysfunction. Erectile dysfunction was mild in 15 (31.9%) patients and moderate in 4 (8.5%) patients. Erectile dysfunction was detected in 9 (37.5%) patients of group 1 and 10 (43.5%) of group 2. When re-questioning 30 days after the start of treatment, erectile dysfunction was noted in 12 (25.5%) patients, that is, 5 (20.8%) patients of group 1 and 7 (30.4%) patients of group 2 ($\chi^2 = 0.569$, $p > 0.1$), and on day 60 from the start of treatment, it was noted in 14 (29.7%) patients, that is, 5 (20.8%) patients of group 1 and 9 (39.1%) of group 2 ($\chi^2 = 1.88$, $p > 0.1$). The difference in the detection of erectile dysfunction in patients of groups 1 and 2 during treatment was not significant.

The tolerability of treatment by patients was satisfactory. In total, 14 negative manifestations were registered during the treatment; all of them were mild and in no case served as a basis for early termination of therapy. The negative manifestations included itching in the anus in six patients (two from group 1 and four from group 2), diarrhoea in three patients (one case from group 1 and two from group 2), headache in two patients (group 2), retrograde ejaculation in two patients (one each from both groups) and flatulence in one patient (group 1). In total, negative manifestations were noted in 5 (20.8%) patients of group 1 and 9 (39.1%) of group 2. Retrograde ejaculation was probably associated with the intake of tamsulosin, whereas other negative manifestations can be explained by the use of rectal suppositories Uroprost-D and indomethacin. Thus, negative manifestations in group 1 were associated with Uroprost-D in 4 (16.7%) patients and indomethacin in group 2 in 8 (34.8%) patients.

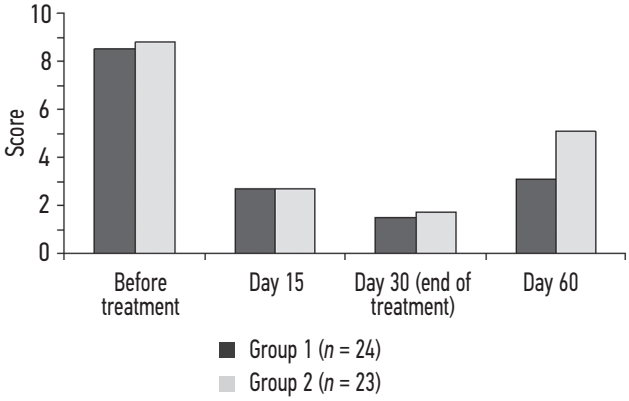

Fig. 5. Dynamics of the total score of the IPSS questionnaire in patients of the 1st and 2nd groups (n = 47)
Рис. 5. Динамика суммарного балла по опроснику IPSS у пациентов 1-й и 2-й групп (n = 47)

DISCUSSION

The results of this study indicate the high efficiency of the peptide bioregulatory drug Uroprost-D in the treatment of CAP, manifested by pain and dysuria. The prescription of Uroprost-D (rectal suppositories) in combination with the alpha-adrenoblocker tamsulosin induced a significant decrease in the severity of pain and urinary disorders. The treatment effect lasted for at least 1 month after the end of the treatment. The clinical efficacy of the combined treatment with Uroprost-D and tamsulosin was not inferior to the combination of indomethacin and tamsulosin and surpassed it in several indicators. Moreover, unlike the use of NSAIDs, the clinical effect of the combination of Uroprost-D and tamsulosin was longer. In addition, better tolerability of treatment was noted in group 1 than in group 2. In this regard, when planning the treatment of patients with CAP/CPPS, the risk of significant side effects with long-term use of NSAIDs must be considered, which may include complications from the cardiovascular system, gastrointestinal tract, blood coagulation system

and kidneys [25, 26]. The clinical use of drugs based on bioregulatory peptides is pathogenetically substantiated and has a fundamental scientific justification. The most significant aim of the therapeutic effect is the correction of the functional activity of cells in the appropriate direction. Peptide bioregulators function as intercellular mediators, maintaining the structural and functional homeostasis of cell populations [14]. Oligomeric peptides penetrate the cell nucleus through the cytoplasm and nuclear membrane. The complementary interaction of these peptides with the promoter regions of genes serves as a signal for transcription, translation and protein synthesis on ribosomes. These processes contribute to a change in the function of various organs and tissues, thereby providing the required therapeutic effect [27].

The clinical application of peptide bioregulators is characterised by several unique characteristics. Their therapeutic effects are not limited only directly to the time of the drug intake but persist for a long time after the end of treatment. A 15-day course of Uroprost-D, relatively short in the present study, had a therapeutic effect for ⩾2 months. Another aspect of the clinical use of regulatory peptides is that their final effect is not promoted with an increase in the amount of a peptide preparation administered into the body, since for each of them, there is a certain limit, after which an increase in the dose no longer enhances the clinical effect. This property is closely related to the distinguishing characteristics of the use of peptide drugs, namely, their lack of dose-dependent clinical effects. A bioregulatory peptide prescribed in the minimum dose can have an incomparably greater clinical effect. All three of these characteristics of the clinical use of bioregulatory peptides are associated with the cascade principle of bioregulation, in which a relatively small amount of a drug triggers a chain reaction that can last for a long time.

The principal factor in CAP pathogenesis is a disorder of microcirculation in the prostate tissue. The ability to improve haemodynamics in the prostate is the main pathogenetic mechanism of the therapeutic effect of prostatic peptides, which include Uroprost-D. The improvement in microcirculation in the prostate gland is due to the high biological activity of prostatic peptides caused by their hypocoagulation and antiaggregation effects and ability to enhance the fibrinolytic activity of blood and improve its rheological properties [15, 16]. The presence of dimethyl sulfoxide in the composition of Uroprost-D, which has penetrant properties, enhances the therapeutic effect of the drug, especially in patients with sclerotic changes in the prostate tissue. The use of Uroprost-D together with an alpha-adrenoblocker has shown its efficiency in relieving both pain syndrome and dysuric disorders in patients with CAP/CPPS, both with inflammatory and non-inflammatory forms of the disease.

CONCLUSIONS

The inclusion of the bioregulatory peptide drug Uroprost-D (rectal suppositories) in the combination therapy of patients with CAP (category III) is clinically effective and pathogenetically substantiated. In these patients, the severity of the pain syndrome and degree of urination disorders are significantly reduced, whereas the therapeutic effect is noted not only during drug use but also after its completion. The clinical efficiency of Uroprost-D is not only inferior to the effectiveness of indomethacin (rectal suppositories) but also surpasses it. Uroprost-D is well tolerated by patients, and it appears to be a pathogenetically reasonable alternative to NSAIDs in these patients. The physiology of the mechanism of the therapeutic action of Uroprost-D and its clinical efficacy enable the recommendation of this drug for use in wide clinical practice for the treatment of patients with patients CAP/CPPS.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

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