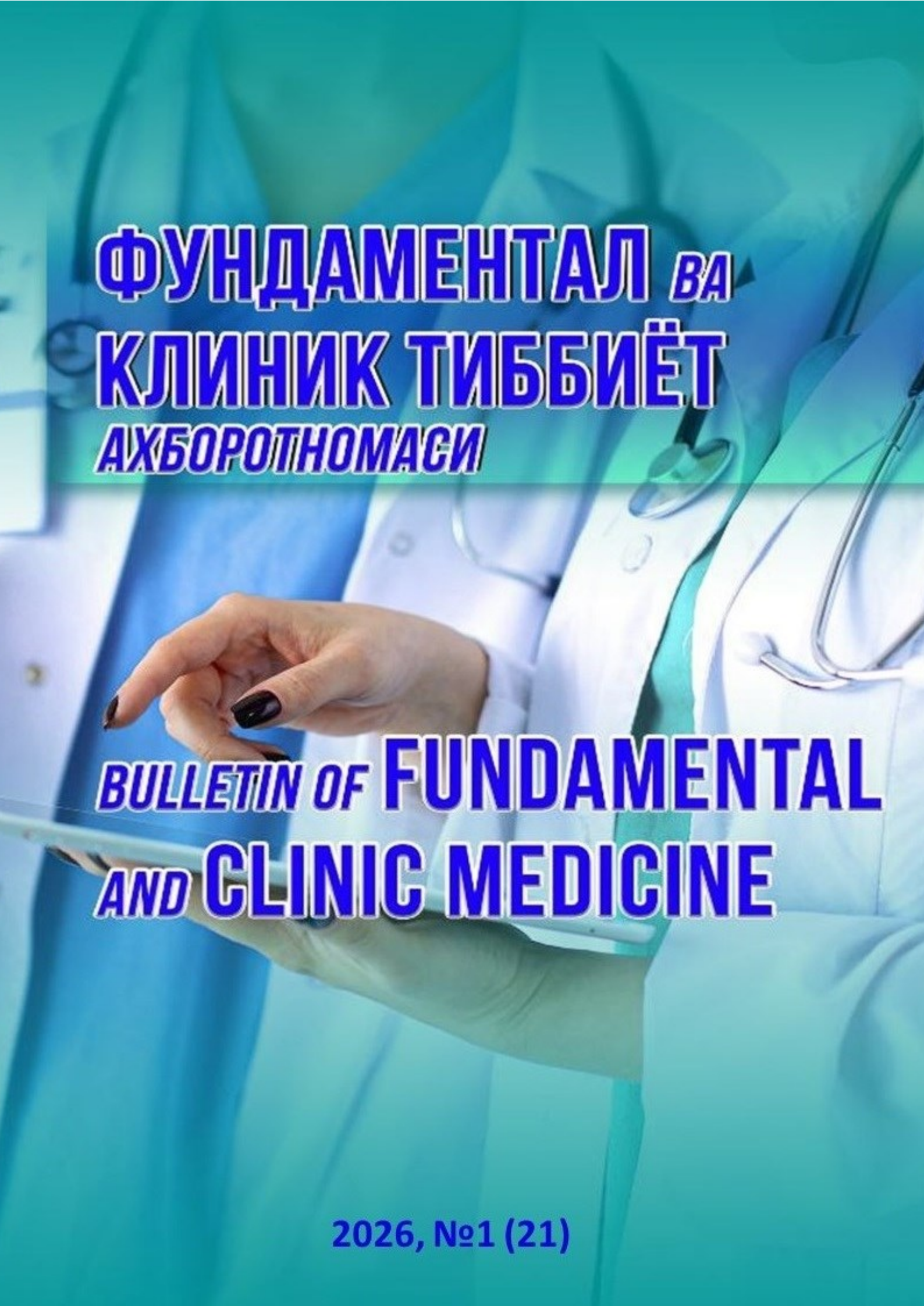

ФУНДАМЕНТАЛ ВА КЛИНИК ТИББИЁТ АХБОРОТНОМАСИ

BULLETIN OF FUNDAMENTAL AND CLINIC MEDICINE

2026, №1 (21)

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РЕСПУБЛИКИ УЗБЕКИСТАН

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CONTEMPORARY APPROACHES TO HORMONAL THERAPY IN MALIGNANT PROSTATE TUMORS

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Resume. *This article analyzes the outcomes of hormonal treatment in 116 patients diagnosed with malignant tumors of the prostate gland. Current androgen deprivation strategies, including surgical castration, the use of luteinizing hormone–releasing hormone (LHRH) analogues and antagonists, as well as antiandrogen agents, are reviewed. Treatment efficacy was evaluated based on clinical and laboratory indicators, along with overall and recurrence-free survival rates. The findings demonstrate the high therapeutic effectiveness of combined hormonal therapy and highlight its potential for optimizing treatment strategies in patients with advanced prostate cancer.*

Keywords: *prostate cancer; hormonal therapy; androgen deprivation; LHRH analogues; antiandrogens.*

ПРОСТАТА БЕЗИ ХАВФЛИ ЎСМАЛАРИНИ ГОРМОНАЛ ДАВОЛАШДА ЗАМОНАВИЙ ЁНДАШУВЛАР

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Резюме. *Ушбу мақолада простата бези хавфли ўсмаси ташхиси қўйилган 116 нафар беморни гормонал даволаш натижалари таҳлил қилинган. Андроген депривацияниng замонавий стратегиялари, шу жумладан жарроҳлик кастрацияси, лютеинловчи гормон-рилизинг-гормон (LHRH) аналоглари ва антагонистлари, шунингдек, антиандроген дори воситаларидан фойдаланиш кўриб чиқилган. Даволаш самарадорлиги клиник ва лаборатор кўрсаткичлар, шунингдек, умумий яшовчанлик ва рецидивсиз яшовчанлик кўрсаткичлари асосида баҳоланди. Олинган маълумотлар комбинацияланган гормонал терапияниng юқори терапевтик самарадорлигини кўрсатади ва унинг кенг тарқалган простата саратони билан оғриган беморларни даволаш стратегиясини оптималлаштириш имкониятларини таъкидлайди.*

Калит сўзлар: *простата бези саратони; гормонал терапия; андроген депривацсия; LHRH аналоглари; антиандрогенлар.*

СОВРЕМЕННЫЕ ПОДХОДЫ К ГОРМОНАЛЬНОЙ ТЕРАПИИ ЗЛОКАЧЕСТВЕННЫХ ОПУХОЛЕЙ ПРЕДСТАТЕЛЬНОЙ ЖЕЛЕЗЫ

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Резюме. *В данной статье анализируются результаты гормонального лечения 116 пациентов с диагнозом злокачественные опухоли предстательной железы. Рассмотрены современные стратегии андрогенной депривации, включая хирургическую кастрацию, использование аналогов и антагонистов лютеинизирующего гормона–рилизинг-гормона (LHRH), а также антиандрогенных препаратов. Эффективность лечения оценивалась на основании клинических и лабораторных показателей, а также показателей общей выживаемости и безрецидивной выживаемости. Полученные данные демонстрируют высокую терапевтическую эффективность комбинированной гормональной терапии и подчеркивают ее потенциал для оптимизации стратегий лечения пациентов с распространенным раком предстательной железы.*

Ключевые слова: *рак предстательной железы; гормональная терапия; андрогенная депривация; аналоги LHRH; антиандрогены.*

Relevance. Prostate cancer (PCa) is one of the most common malignant diseases among elderly men. According to recent epidemiological data, prostate cancer ranks second in incidence among oncological diseases in men in most developed countries. One of the most effective approaches to the treatment of locally advanced and metastatic prostate cancer remains hormonal therapy aimed at suppressing androgens that stimulate tumor growth. Modern hormonal therapy for prostate cancer is focused on blocking or reducing the levels of testosterone, a hormone that plays a key role in the development and progression of prostate cancer

[2,6]. This therapy includes various strategies, such as pharmacological agents that reduce testosterone production or block its action, as well as surgical castration (orchiectomy).

These therapeutic approaches play an important role in controlling tumor progression, reducing clinical symptoms, and enhancing patients' overall quality of life [3]. Androgen receptor antagonists are most often prescribed in combination with androgen deprivation therapy, such as orchiectomy or treatment with luteinizing hormone–releasing hormone (LHRH) agonists. This combined strategy leads to both a reduction in circulating androgen levels and inhibition of residual androgen interaction with androgen receptors, and is commonly described as combined, complete, or maximal androgen blockade [7]. In clinical practice, androgen receptor blockers may also be administered during the initial weeks of androgen deprivation therapy to prevent the transient increase in testosterone levels, known as testosterone flare, that can occur at the start of treatment [1,3,5]. In the United States, approved androgen receptor inhibitors include first-generation agents—flutamide, bicalutamide (Casodex), and nilutamide (Nilandron)—as well as second-generation drugs such as enzalutamide (Xtandi), apalutamide (Erleada), and darolutamide (Nubeqa). Compared with first-generation compounds, second-generation agents exhibit stronger and more selective binding to androgen receptors, resulting in more effective receptor inhibition [4]. Notably, darolutamide does not cross the blood–brain barrier, which may account for its lower incidence of central nervous system–related adverse effects. All androgen receptor blockers are administered orally in tablet form and are intended to be swallowed intact [2,6]. In the United States, androgen receptor blockers approved for the treatment of prostate cancer include first-generation agents such as flutamide, bicalutamide (Casodex), and nilutamide (Nilandron), as well as second-generation agents including enzalutamide (Xtandi), apalutamide (Erleada), and darolutamide (Nubeqa). Second-generation agents bind to androgen receptors and inhibit their activity more potently and selectively compared with first-generation drugs [4]. Darolutamide is the only androgen receptor blocker that does not penetrate the blood–brain barrier, which may result in a lower incidence of central nervous system–related adverse effects. Androgen receptor blockers are administered orally in tablet form and must be swallowed whole [2,6].

Aim of the Study. The aim of this study was to evaluate the effectiveness of various modern hormonal treatment modalities in patients diagnosed with malignant prostate tumors.

Materials and Methods. The study included 116 men aged 57 to 84 years (mean age 71.4 ± 6.2 years) who were treated at an oncology center between 2020 and 2024. All patients had a confirmed diagnosis of prostate cancer at stages T2–T4N0–1M0–1, established based on histological examination of biopsy specimens and MRI/CT imaging data.

Depending on the hormonal treatment modality used, patients were divided into the following groups: - **Group I** (n = 32): surgical castration (orchiectomy); - **Group II** (n = 38): therapy with LHRH analogues (goserelin, leuprorelin); - **Group III** (n = 29): combined androgen blockade (LHRH analogue + antiandrogen); - **Group IV** (n = 17): treatment with LHRH antagonists (degarelix) in aggressive forms of prostate cancer.

Treatment efficacy was assessed based on prostate-specific antigen (PSA) dynamics, overall survival, progression-free survival, disease progression rate, and incidence of adverse events. Quality of life was subjectively evaluated using the EORTC QLQ-C30 questionnaire and the prostate cancer–specific PR25 module.

Results. Before treatment, the mean PSA level was 74.2 ± 15.3 ng/mL. During hormonal therapy, a greater than 50% reduction in PSA levels within the first three months of treatment was observed in 88% of patients. The most pronounced decrease was noted in Group III (combined androgen blockade). Adverse events were reported in 34 patients (29.3%), primarily presenting as hot flashes, decreased libido, and fatigue. Treatment regimens involving LHRH antagonists demonstrated the best tolerability profile.

Table 1.

Survival Rates of Patients with Prostate Cancer According to the Type of Hormonal Therapy

Treatment Group	Overall 3-year Survival, %	3-year Recurrence-Free Survival, %
Group I – Orchiectomy	**64,3%**	**48,1%**
Group II – LHRH analogues	**71,1%**	**55,3%**
Group III – Combined hormonal blockade	**78,6%**	**66,7%**
Group IV – LHRH antagonists	**69,2%**	**58,8%**

Thus, the best overall survival and recurrence-free survival outcomes were observed in patients who received combined hormonal therapy. The study included 116 patients diagnosed with prostate cancer (PCa)

who underwent hormonal therapy using different treatment modalities. The mean age of the patients was 71.4 ± 6.2 years. In the majority of patients (78.4%), the disease was diagnosed at clinical stages III–IV. The mean PSA level before treatment was 74.2 ± 15.3 ng/mL. During hormonal therapy, a significant reduction in PSA levels was observed in most patients after 4 weeks of treatment. After 3 months of therapy, 88% of patients demonstrated a greater than 50% decrease in PSA levels compared with baseline. The most pronounced PSA reduction was recorded in Group III (combined androgen blockade), where 93% of patients achieved a ≥50% reduction, and 65% achieved a ≥90% reduction in PSA levels. In Group II (LHRH analogues), a comparable effect was observed in 87% of patients; in Group IV (LHRH antagonists), in 88%; and in Group I (orchiectomy), in 81% of patients. Disease progression was most frequently observed in Group I (9 cases) and Group II (8 cases), followed by Group III (5 cases) and Group IV (2 cases). In patients with disease progression, treatment with abiraterone or enzalutamide was initiated. Adverse events were reported in 34 patients (29.3%). The most common adverse effects included hot flashes (22.4%), decreased libido and sexual dysfunction (18.1%), fatigue and asthenia (15.5%), and gynecomastia (5.2%). The lowest incidence of adverse events was observed in Group IV (LHRH antagonists), where adverse effects were reported in only 23.5% of patients. Therapy was most poorly tolerated in Group I, where psycho-emotional disturbances, osteoporosis, and pronounced asthenia were more frequently recorded. The highest preservation of social functioning and overall health status was observed in patients receiving LHRH antagonists and combined therapy, whereas the worst emotional functioning scores were noted in the orchiectomy group.

Discussion. The results indicate that modern hormonal therapy approaches demonstrate high efficacy in the treatment of advanced prostate cancer. Combined androgen blockade showed the most favorable outcomes in terms of PSA reduction and survival, confirming the relevance of a multimodal therapeutic approach. The LHRH antagonist degarelix deserves special attention, as it provides rapid testosterone suppression without an initial testosterone surge. However, the development of castration-resistant prostate cancer remains a significant clinical challenge, necessitating the development of strategies for sequential or combined use of hormonal and targeted therapies.

Conclusion. Hormonal therapy remains a key component in the management of advanced prostate cancer. Combined androgen blockade demonstrates the highest therapeutic efficacy and should be considered a preferred approach in patients with contraindications to surgical intervention. Further studies aimed at therapy individualization and overcoming hormonal resistance are required.

LHRH agonists remain the most widely used form of androgen deprivation therapy, offering prolonged suppression of testosterone activity following a single, well-tolerated injection lasting up to 6 months. As monotherapy, certain agents achieve extremely low testosterone levels, including nadir values below 5 ng/dL. Newly developed treatments utilize enhanced mechanisms of action or improved drug delivery systems to further optimize existing therapeutic approaches. In addition, advances in genetic testing open new opportunities for personalizing treatment strategies to optimize efficacy and safety.

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