ISSN 2518-1432 (Online); ISSN 2227-4782 (Print) https://doi.org/10.21856/j-PEP.2023.4.07

ОГЛЯДИ

FERTILITY FACTORS. D-HORMONE IN PREVENTION OF REPRODUCOPATHIES CAUSED BY BENIGN PROSTATIC HYPERPLASIA (literature review)*

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In recent years the number of patients suffering from benign prostatic hyperplasia (BPH) is increasing that makes a contribution to the quantity of infertile couples. As well known, sex function is very sensitive to negative factors which can change reproductive as well as copulative component of men's health. The features of modern life style and prolonged stress may cause the hormonal changes — the declining of testosterone (Ts) secretion, increasing of gonadotropins, corticosteroids and prolactin (PRL) concentrations, disturbance of androgen-estrogen ratio, which lead to reproductive system diseases, sexual disorders and infertility [1–3].

It was previously thought, that BPH mostly occurred in elderly men, but, according to the world statistic data, 20–40 % of 41-50-year-old person, approximately 50 % of 51-60 — year-old, about 60 % of men aged above 60 years and majority (80 %) of men over 80 years of age are suffering from BPH. According to epidemiological data in 2016 year there were 1082 cases of BPH per 100.000 members of male population over 18 years of age in Ukraine [4–6]. The number of men under 50 which have got or will get these diseases will grow, because factors listed above are occurring more frequent in the modern life [4, 7]. The impact of these factors which lead to decreasing of men sex hormones production, the disturbance of metabolism and other disharmonious conditions will cause the appearance of BPH in men at younger ages.

* The work was carried out in accordance with the scientific theme of the State Institution «V. Danilevsky Institute for Endocrine Pathology Problems of the National Academy of Medical Sciences of Ukraine» «The definition of role of D-hormone in the prophylaxis of benign prostatic hyperplasia and grounding of methods of correction of reproductopathies caused by this disorder» (State registration number 0122U200369).

The institution that finances the study is the National Academy of Medical Sciences of Ukraine.

The authors assume responsibility for the published work.

The authors guarantee absence of competing interests and their financial interest when carrying out the research and writing the article.

The manuscript was received by the editorial staff 01.09.23.

As it is well-known, the prostate gland (PG) plays an important role in men's fertility [8]. Being additional sex gland PG has endocrine function: it takes part in the transformation of Ts into dihydrotestosteron (DHT) — more active androgen. PG has exocrine function too: it is responsible for the production of prostate fluid which is enriched with proteins, enzymes, lipids, amines and metals ions, in particular, zinc ions, that make fluid environment slightly acidic and support the vitality of spermatozoon [9]. Prostate fluid protects sperm cells by declining acidic environment in the urethra and enhancing sperm motility. Moreover, prostatic acid phosphatase takes part in the sperm's nutrition by hydrolysis of phosphorylcholine into choline.

PG is the target for some widespread diseases which influence the reproductive capacity of men of different ages. The PG diseases can impact on sperms' functioning, and therefore, on the men fertility in young men as well as in aged. Some factors may contribute to this condition: the core role of Zn^{2+} and citrates in the regulation of homeostasis of gland epithelium and in ejaculation; the impact of PG bacterial inflammation on man fertility; and potential role of the PG inflammation in the hyperplastic processes' development and carcinogenesis of this organ [8].

The pathogenesis of BPH is connected with disturbances of regulation in the hypothalamo-hypophyseal system and with the changes of the regulatory signals intensity which go to the reproductive organs. The central pathogenic links of this pathology' development are: the declining of efficacy of hypothalamus functioning regulation which carries out on the principle of feedback; the changes of the pituitary gland cells sensitivity to the releasing hormones of hypothalamus and disbalance between estrogens and androgens production. At the organs' level the development of BPH is caused by increasing of 5α-reductase activity which catalyzes the conversion of testosterone to dehydrotestosterone, intensifying of synthesis of tissues' growth factors, increasing of expression of androgenic and α-1-adrenoreceptors. [10, 11]. In addition to gonadotropins, PRL (one of hormones of adenohypophysis) has a significant impact on the BPH development. Its hypersecretion is considered to be the substantial cause of the appearance of hyperplastic age-related changes of PG. PRL stimulates proliferation and acts as an androgen-depended suppressor of the PG epithelium apoptosis which leads to the PG hyperplasia. In fact, the increasing of the PRL level under stress and its important ethiopathogenic role in the reproductive capacity declining are generally accepted now [12, 13].

The experimental introducing of dopamine receptors antagonists such as sulpiride for BPH modeling leads to the PRL concentration increasing and declining of gonadotropins releasing [14, 15]. «Sulpiride model» is broadly used in the experimental endocrinology for studying prostate-active medicines suitable for BHP treatment [16]. This model is characterized by sex hormones disbalance' and inflammation processes' development in rats. Under this condition the development of BPH is linked with the disturbance of Ts synthesis in the testicles due to insufficiency of PG functioning and increasing of PRL and E_2 concentrations which provoke proliferative changes in this organ.

Long-term administration of sulpiride (neuroleptic, dopamine receptors antagonist) induces PRL hypersecretion which causes the increasing of proliferation of glandular epithelium of PG. In this case, the pathogenesis of acinar hyperplasia is conditioned by increasing of 5α-reductase activity and epithelial cells sensitivity; in 50 % of cases the pathology develops under the condition of chronic prostatitis (CH) and lowered sensitivity to androgens [14, 15].

Considering the fact that PG growing, differentiation and functioning are controlled by sex hormones, the most of BPH' pathogenesis theories are focused on the hormone regulation. This regulation is based on the presence of androgen (AR) and estrogen receptors (ER) as well as these hormones production in basal and luminal cells of PG. The main hormone, regulated PG growing, is 5α-DHT, which is synthetized from Ts in the epithelium and stromal cells of gland [17, 18]. BPH may exactly develop in these epithelial and stromal cells due to their excessive growing.

Taking into account the main cause of BHP developing is disbalance of androgens, the so-called «Testosterone model» or «Testosterone

induced model» have been proposed and broadly used [19]. Thus, it has been described that BHP may be induced in rats' males of Sprague-Dawley line by intramuscular introduction of Ts propionate in dose of 5mg/kg during 14 days [20]. The considerable increasing of prostate specific antigen (PSA) concentration in rats with BHP has been determined on the 14th day of the experiment, whereas testicles mass and semen quality were significantly worse than in control rats.

The Testosterone model is used in other experimental animals, for example, in mice by injection of Ts propionate in dose of 20 mg/kg during 30 days [21]. The hyperplasia of PG and abnormal proliferation of epithelial and stromal cells with signs of inflammation which caused acinar stenosis have been detected to be the histopathological results of this modeling.

The using of subcutaneous Ts and E_2 implants with delayed release of (Tc + E_2) for inducing difficulty urinating which resembles similar process in aging men with BHP is another option of such modeling [22].

It is reported about spontaneous BHP (age-related spontaneous benign prostatic hyperplasia) in aged rats (> 12 months) [23].

During experimental modeling the gland inflammation (prostatitis) develops with BHP and often combines with urethritis and vesiculitis which lead to the spermatogenesis disturbances [14] as well as in clinical practice when disorders of reproductive function are detected in patients. It can be sexual disorders, spermatopathies, hypofertility occurred due to increased production of active oxygen radicals with the inflammation caused by prostatitis [24, 25]. The morphological sperm cells changes and DNA fragmentation may appear due to increased oxidative stress and hormonal disbalance. It has experimentally been shown that BHP has decreased sperm DNA integrity, has increased the mitochondrial activity and changed the pattern of sperm movement [26]. Thus, the deterioration of sperm quality in dogs with BHP mainly caused by changes of sperm kinetic and is accompanied by considerable changes of Ts and estrogens concentrations [27].

The absence of hormonal balance leads to increasing of androgen receptors amount in PG enhancing the effect of Ts [28] which is the main cause of noticeable transformation of Ts into DHT under the action of 5α-reductase [29, 30]. Angrimani D. S. et al. (2020) [27] summaries, that the increasing of DHT concentration causes PG changes such as hypertrophy and hyperplasia of glandular cells, angiogenesis [30] and local oxidative stress in men [31] and in animals [32]. In this case, the disturbance of spermatogenesis in dogs with BHP is considered to be the indirect consequence of hormonal disbalance, but not the direct result of testicles morphological changes, because there weren't any significant histological findings which would have explained the considerable decreasing of sperm cells concentration and higher percentage of little sperm defections. Moreover, the changes of sperm motility in dogs with BHP may be linked with lowered secretion of Leydig's cells [27]. Sperm quality degradation can impact fertility and reduces the likelihood of insemination *in vitro*. In addition, the disturbances of ejaculation are occurred in almost half of patients with the symptoms of low urinary tract linked with BHP [33].

It is well-known that life style which becomes now more complicated by external insuperable circumstances is essential in the development of BHP [34, 35]. The prevention and treatment of this pathology is not only medical, but serious social problem too. Nowadays, taking into consideration results of the investigations of pathogenesis of hyperplastic processes in PG and mechanisms of drug action, medical treatment of BHP as well as surgery take an important place among other methods of its sanation [36, 37].

The BHP therapy usually consists of complex of therapeutic measurers such as: the use of α_1-adrenoblockers (Doxazosin, Tamsulosin, Silodosin), inhibitors of 5α-reductase, phosphodiesterase type 5 inhibitors, anticholinergics and norepinephrine agonists (3-ß agonists). However, the application of this therapy is accompanied by numerous side effects (decreasing of sperm production, gynecomastia etc.) which associated with the consequences of long-term dilatation of small vessels [6, 8, 17].

According to the international urological associations' guidelines, for BHP therapies are

recommended drugs of such pharmacotherapeutic groups as follows: α_1-adrenomimetics, inhibitors of 5α-reductase, anticholinergics, anti-hormonal agents, non-steroidal anti-inflammatory drugs. Systemic drug therapy has significant number of side effects. For example, inhibitors of 5α-reductase may cause disturbances of reproductive system. This is not desirable, because, statistically BHP is occurred in men of active reproductive age and decrease in sexual activity, impaired fertility affect the quality of life. However, this group of drugs continues to be used as surgery alternative due to positive results of treatment [38].

Scientific researchers have increasingly focused on the searching of substances for BHP treatment among plant-based remedies which haven't disadvantages of systemic prostate protectors. The BHP phytotherapy is very popular in word. The herbal preparations based on Saw Palmetto fruits (*Serenoa repens*), bark of African plum tree (*Piogenum Africanum*), Nettle root extract (*Urtica dioica and Urtica urens*), plant pollen extract, Prickly Pear flowers extract, pumpkin seed oil etc. are used for BHP treatment [39]. It is necessary to point out, that pant-based drugs have got wider therapeutic range and are safer than other therapeutic groups. They often use as a drug of choice for men under the age of 55. However, they are not considered to be more effective, than α_1-adrenomimetics and inhibitors of 5α-reductase, because they haven't been studied enough. (Zaichenko H.V., 2016). The combined drugs which consist of some active pharmaceutical ingredients of different mechanisms of action and application of medicines of different pharmaceutical groups are considered a promising [17].

Thus, the plant-based drugs can be distinguished among anti-inflammatory and immunomodulating remedies. Serenoa repens fruit extract (Pristamo® Uno) is widely used for CP and BHP treatment, although, data obtained are controversial. The pharmaceutical composition based on Nettle and Broccoli extracts is created; its inhibition of BHP has been detected [40].

All listed above is the base of searching of new drugs for BHP prevention and treatment. Accumulated during decades data indicate BHP traditional therapeutic methods are not always effective. The application of antibiotics and α1-adrenoblockers under the condition of nonspecific chronic prostatitis hasn't changed the NIH — CPSI (National Institutes of health Chronic Prostatitis Symptom Index, USA), although the positive effect of the myorelaxants application is detected [41].

As it has been pointed out earlier, the prevention and treatment of PG diseases have not only medical, but social importance too. The prostate gland-linked declining of the reproductive function may induce by different causes which are often connected with the disturbances of gland structure and functioning. At the same time, the studying of D-hormone influence on the organism is the topical problem now, because its activity in men is closely associated with the pathogenesis of androgen deficiency and hypofertility [42, 43].

Data obtained show that vitamin D level defines ejaculate amount and quality in men [44, 45] (including sperm cells motility and their morphology [46, 47]), and ripening of spermatozoon. The correlation between low concentration of vitamin D and increased quantity of motile and morphologically normal sperms has been determined. The positive correlation between the volume of ejaculate and fructose concentration in semen fluid has been also detected [48]. The deficiency of vitamin D is associated with lower Ts/E_2 ratio in young men and with the decreased sensitivity of Leydig's cells after hCG stimulation in men with gonad dysfunction [49].

Several investigations accomplished in animals and men have detected the relation between vitamin D level and sex hormones production [49]. The lack of vitamin D has caused the disturbances of spermatic duct ripening, the declining of testicles mass and sperms concentration [50]. It has been experimentally shown that organism' normal saturation by vitamin D has led to significant improvement of spermatogenesis under the condition of experimental reproductopathies [51, 52].

Literature data as for evaluating of vitamin D using in men have demonstrated wide variability in methods of investigations, contingent of patients, reference values and methods of introduction of vitamin D as well as its

metabolites. All of these data require further investigations.

Vitamin D belongs to the oil soluble sekosteroid group. Sekosteroid is the molecule which structure is similar to steroids, but its steroid ring is ripped. There are several chemical forms of vitamin D in the nature, however, the most important forms for human organism are ergocalciferol (vitamin D_2) and cholecalciferol (vitamin D_3) which are chemically differed in their side chains. These structural differences change the binding to the carrier protein, in particular, to the vitamin D-binding protein. The metabolism of this chemical forms of vitamin D is also differed, but the biological activity of these derivates is similar [53, 54].

The frequency of vitamin D deficiency among «men' urological population» may confirm the link between BHP and vitamin D. Vitamin D inhibits RhoA/ROCK pathway complete with cyclooxygenase-2 expression and prostaglandin E_2 production in the stromal cells of PG. It has been detected that the increasing of vitamin D consumption with food or dietary supplements strongly correlates with the declining of BHP frequency, moreover, vitamin D analogues intake decreases the PG volume in patients with this pathology. Preclinical trials have shown vitamin D inhibits not only PG cells' proliferation under the condition of BHP, but also when proliferation is induced by such stimulating molecules as IL-8, Des (1–3) IGF-1, Ts and DhTs [7, 55].

It has been additionally described that cholecalciferol regulates steroid genesis and mitigates the age-related declining of testicles activity on the model of old rats [56]. The results of the investigations in vivo and in vitro have detected that vitamin D_3 directly regulates testicles steroids markers. The application of vitamin D_3 has also increased CYP19A1 activity and inhibited AR expression in testicles of old rats as well as health animals. These results have confirmed that indirect estrogen activity may lead to the spermatogenesis improvement in old animals. In addition, it is conceivable, that cholecalciferol can protect the testicles in old rats and unchanged spermatogenesis in health males which received vitamin D_3 may be the result of balance between estrogens and androgens action.

Nowadays, vitamin D is considered to be the modulator of reproductive system functioning [43, 57].

The androgens receptors as well as vitamin D receptors (VDR) have been detected in normal PG and under the condition of BHP. This vitamin-hormone provides its effects through the binding to VDR-receptor, which is transcription factor and takes part in the regulation of genes transcription after its ligand-depended activation [43, 58]. The potential chemical preventive effect of vitamin D prohormone has been demonstrated by the investigations carried out in cells culture in vitro and in the animals in vivo as well as by epidemiological and clinical trials [59, 60]. In addition to its classic ability to regulate the calcium metabolism and bone condition, vitamin D can inhibit tumor developing in tissues, including PG [59]. $1,25(OH)_2$ D, which is an active vitamin D metabolite in the PG cells, can exhibit antiproliferative, proapoptotic and anti-inflammatory effects.

The antiinflammatory activity of $1,25(OH)_2D$ is manifested by IL-6 and IL-8 inhibition in human PG cells. During investigation of prostatitis in mice in vivo, elocalcitol, the analogue of $1,25(OH)_2D$, has declined inflammatory infiltration, nitrogen oxide signaling and cytokines production [59].

Although, it hasn't been earlier reported about VDR and vitamin D genes expression according to the cells type in PG tissue, and taking into account the importance of interaction of stromal and epithelial cells and expression of vitamin D receptor (VDR) by both cell types, it has been suggested that stromal and epithelial cells have got unique functions in the mediating of vitamin D activity in prostate gland [59].

The expression levels of VDR and CYP24A1 enzyme of men's sperm, which inactivates vitamin D, are the positive prognostic markers of sperm quality and higher in health men than in infertile. VDR mediates the increasing of spermatozoa motility and induces the acrosome reactions [61].

The application of rectal gel based on Prostatilen and vitamin D_3 in animals with experimental prostatitis has considerably decreased the number of pathologically changed sperm cells and, also, has been more effective for im-

proving males' copulative function than separate administration of Prostatilen gel applied per rectum and vitamin D_3 used per os. The using cholecalciferol per os significantly potentiates prostatprotective properties of Prostatilen under the condition of experimental prostatitis [62].

The results of this investigation can be the ground of vitamin D using to be the pharmaceutical composition amidst basic therapy which can improve the efficacy of correction of the reproductive function disturbances caused by BHP. The ability of complex application of cholecalciferol to restore the reproductive capacity with chronic prostatitis caused by inflammation or trauma makes it possible to use D-hormone for improving of PG structure and reparative function in patients with BHP, to recover men' health under the condition of this pathology.

The cross-sectional clinical trials have confirmed the link between 25-hydroxivitamin D (25(OH)D) serum level and sperm quality is positive in fertile men as well as in infertile. However, it should be determined whether this link shows causal effect, because vitamin' D influence on the gonad function can be carried out through other endocrine factors which are regulated by vitamin D [61].

Some authors recommend using cholecalciferol to prevent recurrent infection of urinary tract in patients with BHP. The application of vitamin D can prevent the patients which received Tamsuloside from this complication without addition side effects [63].

Any investigations haven't found out connection between increased intake of vitamin D and negative consequences [55, 64].

Therefore, the estimation of literature data as for vitamin D impact on the PG functioning and BHP development has confirmed the topicality and perceptivity of studying of vitamin D using for treatment and prevention of hypofertility. The further investigations of the vitamin D role in therapy and prophylaxis of reproductive system' pathologies developed due to or amid BHP are needed.

The application of vitamin (hormone) D to be the monotherapy or in pharmaceutical composition and introduction of cholecalciferol into usual schemes of treatment can enhance the effectiveness of sanation and allow for the possibility of the reproductive capacity recovering in men with BHP with D-hypovitaminosis as well as without it.

One of the main causes of men' fertility deterioration, in other words the cause of hypofertility, are the PG diseases, in particular, BHP, which is considered to be the most widespread pathology of men' reproductive system. The recovery of health in men with BHP is not effective enough which explains the significance of developing of new drugs and using of new treatment schemes for correction of BHP and its consequences for men' reproductive function. The searching of new methods of influencing the reproductive function through the normalizing of structure and functioning of PG is the base for developing of new medicines — prostate protectors which contain vitamin-hormone D, or new schemes of combined application of cholecalciferol with drugs of base BHP therapy.

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ЧИННИКИ ФЕРТИЛЬНОСТІ. D-ГОРМОН У ПРОФІЛАКТИЦІ РЕПРОДУКТОПАТІЙ, ОБУМОВЛЕНИХ ДОБРОЯКІСНОЮ ГІПЕРПЛАЗІЄЮ ПЕРЕДМІХУРОВОЇ ЗАЛОЗИ (огляд літератури)

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Згідно зі статистичними даними поширеність доброякісної гіперплазії передміхурової залози (ДГПЗ) зростає, бо сучасне стресогенне життя викликає дисбаланс статевих гормонів та інші дисгормональні стани, що спричиняє виникнення патології в більш молодому віці.

Патогенез ДГПЗ пов'язаний з порушеннями гіпоталамо-гіпофізарної системи та зміною інтенсивності регуляторних сигналів, що надходять до репродуктивних органів. До центральних патогенетичних ланок її розвитку відносять зниження ефективності регуляції функцій гіпоталамуса, що здійснюється за принципом зворотного зв'язку, зміну чутливості клітин гіпофізу до рилізинг-гормонів та дисбаланс статевих гормонів. Окрім гонадотропінів, на розвиток ДГПЗ впливає пролактин, гіперсекреція якого викликає вікові гіперпластичні процеси у простаті. Збільшенню рівня пролактину та зменшенню вивільнення гонадотропних гормонів сприяє введення блокаторів дофамінових рецепторів, наприклад: сульпіриду. «Сульпіридна модель», широко використовується в експериментальній ендокринології для вивчення простатотропної активності ліків і характеризується розвитком запального процесу та диспропорцією статевих гормонів. Виникнення патології пов'язано з порушенням синтезу тестостерону сім'яниками, недостатньою функцією простати, збільшенням вмісту пролактину та естрадіолу, що провокує проліферативні зміни. Дисбаланс андрогенів є провідною причиною ДГПЗ, тому «тестостеронова модель» цього захворювання із використанням імплантатів тестостерону та естрадіолу та з уповільненим їхнім вивільненням широко застосовується для дисфункції сечовипускання у щурів, яке нагадує таке у старіючих чоловіків при доброякісній гіперплазії простати.

На тлі ДГПЗ виникає простатит, який викликає порушення сперматогенезу при експериментальному моделюванні та в клініці, де у таких хворих діагностують сексуальні розлади, сперматопатії, гіпофертильність.

Традиційні методи терапії ДГПЗ не завжди ефективні та спонукають дослідників шукати нові шляхи лікування гіпофертильності при цій простатопатії. Так, існують дані про те, що збільшення споживання вітаміну D корелює зі зниженням поширеності ДГПЗ, об'єму залози та проліферацією клітин простати у пацієнтів із даною патологією. Рівень вітаміну D впливає на якісні та кількісні параметри еякуляту. Дефіцит вітаміну D асоціюється з нижчим співвідношенням статевих гормонів у молодих чоловіків і нижчою чутливістю клітин Ляйдігу до стимуляції хоріогоніном. В експерименті показано, що холекальциферол регулює стероїдогенез, пом'якшуючи дію вікового зниження активності сім'яників, відіграє захисну роль у яєчках старих тварин, а незмінний сперматогенез у нормальних самців, які отримували вітамін D_3, може бути наслідком балансу між дією естрогенів та андрогенів. У простаті у нормі та при гіперплазії знайдено рецептори не тільки до андрогенів, а й до вітаміну D. На додаток до своєї класичної функції в гомеостазі кальцію та здоров'ї кісток, вітамін D пригнічує ріст пухлин різних тканин, включно з простатою. У метаболітів вітаміну D виявлено антипроліферативний, проапоптотичний та протизапальний ефекти. Використання D-гормону в експерименті потенціює специфічні властивості простатопротекторів, відновлює репродуктивний потенціал за умов хронічного простатиту як запального, так і травматичного ґенезу.

Вищенаведене дає можливість сподіватись на позитивну роль D-гормону у регуляції роботи простати і генеративної функції у особин із ДГПЗ, відновлення фертильності за умов цієї патології.

Пошук літератури для огляду проведено за базами даних PubMed, SeinceDirect, Europa PMC, BMC, MedLine тощо.

Ключові слова: ендокринологія, андрологія, огляд, вітамін D, репродуктивні розлади, доброякісна гіперплазія передміхурової залози.

FERTILITY FACTORS. D-HORMONE IN PREVENTION OF REPRODUCOPATHIES CAUSED BY BENIGN PROSTATIC HYPERPLASIA (literature review)

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In accordance with the statistical data, the spreading of benign prostatic hyperplasia (BPH) is increasing, because modern stressful lifestyle causes sex hormones disbalances and other dyshormonal conditions which lead to pathologies' development at younger ages.

The pathogenesis of BPH is connected with disturbances of regulation in the hypothalamo-hypophyseal system and with the changes of the regulatory signals intensity which go to the reproductive organs. The central pathogenic links of this pathology' development are: the declining of efficacy of hypothalamus functioning regulation which carries out on the basis of feedback; the changes of the pituitary gland cells sensitivity to the releasing hormones of hypothalamus and disbalance of sex hormones. In addition to gonadotropins prolactin has a significant impact on the BPH development. Its hypersecretion causes the development of hyperplastic age-related changes in prostate gland. The introduction of dopamine receptors antagonists such as sulpiride causes the increasing of prolactin concentration and declining of gonadotropins releasing. «Sulpiride model» is broadly used in the experimental endocrinology for studying prostate-active drugs and is characterized by sex hormones disbalance' and inflammation processes' development. The development of the pathology is linked with the disturbance of testosterone synthesis in the testicles, insufficiency of prostate gland functioning and increasing of prolactin and estradiol concentrations which provoke proliferative changes. The androgens disbalance is the main cause of BHP development, therefore, the «Testosterone model» based on testosterone' and estradiol' slow releasing implants is broadly used for modeling of urination disturbance in rats which imitates the same condition in elderly men with benign prostatic hyperplasia.

The prostatitis, which developed under the condition of BHP, causes the disturbances of spermatogenesis during experimental modeling and in the clinical practice when spermatopathies, sexual disturbances and hypofertility are diagnosed in patients.

The traditional BHP therapeutic methods are not always effective and the new therapeutic approaches of hypofertility caused by prostate gland pathologies are developed by investigators. Thus, there are data about correlation between increased vitamin D consumption and decreasing of BHP spreading, between gland volume and cells proliferation in patients with this pathology. Vitamin D level influences the quantity and quality of ejaculate. The deficiency of vitamin D is associated with lower proportion of sex hormones in young men and choriogonin sensitivity of Leydig's cells to be diminished. It has been experimentally shown that cholecalciferol regulates steroid hormones genesis, mitigates the age-related declining of testicles activity, protects the testicles in old animals and the unchanged spermatogenesis in normal males which received vitamin D_3 can be considered to be the result of estrogens and androgens balance. The androgens receptors as well as vitamin D receptors have been found in prostate gland in health males and in those with hyperplasia. In addition to its classical function in calcium homeostasis and bones health, vitamin D inhibits tumor growth in different tissues including prostate gland. Vitamin D metabolites have been determined to be anti-inflammatory, proapoptotic and antiproliferative. D-hormone application potentiates the specific properties of prostate gland protectors, recovers reproductive capacity under the condition of experimental chronic prostatitis of inflammatory genesis as well as traumatic.

All facts listed above allow to confirm the positive role of D-hormone in the regulation of prostate gland and reproductive function in patients with BHP and recovering of fertility under the condition of this pathology.

The literature search for this review has been carried out on databases PubMed, Science Direct, Europa PMC, BMC, MedLine etc.

Keywords: endocrinology, andrology, review, vitamin D, reproductive disturbances, benign prostatic hyperplasia.