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FUNCTIONAL STATE OF TESTICLES AND VITAMIN D LEVELS IN THE BLOOD OF YOUNG MEN WITH PROSTATE DISEASES AND INFERTILITY*

V. O. Bondarenko [1], Ye. M. Korenieva [1], Ye. I. Skornyakov [1], N. M. Brechka [1,2], I. O. Bielkina [1], N. P. Smolienko [1], A. S. Minuhin [3]

[1] SI «V. Danilevsky Institute for Endocrine Pathology Problems of the NAMS of Ukraine», Kharkiv, Ukraine;
[2] Private establishment of higher education «Kharkiv institute of medicine and biomedical sciences», Kharkiv, Ukraine;
[3] LLC «Instinct of the Sun», Kharkiv, Ukraine
eugenia_koreneva@i.ua

One of the most common causes of male reproductive dysfunction is chronic prostatitis (CP) [1], which is more common in men under 50 years of age [2]. Meta-analysis of the literature has shown that CP is associated with decreased sperm quality, increased antisperm antibodies, and high levels of sperm DNA fragmentation [3], which are the cause of male infertility. In turn, benign prostatic hyperplasia (BPH) is diagnosed in 30-40% of men in the fourth decade of life, in the formation of which, as in CP, local inflammation in the prostate gland plays a role [2, 4].

Studies conducted in the last decade have shown that sperm quality can be affected by blood levels of vitamin D (Vit. D). It has been shown that under conditions of D-hypovitaminosis, spermogram parameters deteriorate [5, 6]. During Vit. D deficiency, men may have low levels of testosterone (T) in the blood and signs of androgen deficiency, which negatively affects spermatogenesis [7]. The use of cholecalciferol can improve sperm quality and contribute to an increase in T levels in the blood [8]. Meanwhile, experimental and clinical studies show that in the prostate, Vit. D exhibits anti-inflammatory and antiproliferative effects [6, 9], helps reduce signs of hypogonadism in BPH [10]. When modeling CP, the use of cholecalciferol has a positive effect on the restoration of the histostructure of the prostate and improves the fertilization ability of sperm [11].

However, as of now, there are no data on the specifics of changes in spermatogenic and endocrine functions of the testicles in men with infertility due to CP and BPH depending on the level of Vit. D in the blood. This constituted the aim of our study.

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MATERIALS AND METHODS

We analyzed the indicators of the functional state of the testicles in 61 men aged 24–45 years who were examined for infertility within marriage.

Anamnesis and clinical examination provided grounds for establishing signs of CP in 32 men and BPH in 31 patients. The patients had no endocrinopathies, hypogonadism, or varicocele. All subjects were measured for body mass index (BMI), analyzed for sperm parameters according to WHO recommendations [1], and also for T, estradiol (E_2), and vit. D levels in the blood. T and E_2 were determined by enzyme immunoassay (Kits LLC «HEMA», Ukraine). The level of vit. D in the blood was determined using kits (25-OH Vitamin D (total) ELISA, DRG Germany for enzyme immunoassay. The content of hormones in the blood was determined at different times of the year.

Similarly, the hormonal status and blood levels of vitamin D were analyzed in 27 clinically healthy men with spermogram parameters meeting the WHO norm of the same age, who formed the control group.

The studies were conducted in compliance with the principles of the Helsinki Declaration of Human Rights, the Council of Europe Convention on Human Rights and Biomedicine, and the current legislation of Ukraine. The study protocol was approved by the Medical Ethics Committee of the SI IEPP.

Statistical analysis of the obtained data was carried out by the method of variational statistics using the standard statistical calculation the Statistica 10.0 software package. The arithmetic mean and its error ($\bar{X} \pm S_{\bar{X}}$) were calculated. The normality of the distribution of variables was determined using the Shapiro-Wilk test. The significance of differences between groups was assessed using the chi-squared (χ^2) test. The presence of correlations was determined using the Pearson correlation coefficient (r). Calculations were considered statistically significant if $p \leq 0.05$.

RESULTS AND THEIR DISCUSSION

According to the latest recommendations of the Endocrine Society, the division of vitamin D levels in the blood into categories of sufficiency, insufficiency, and deficiency is currently considered inappropriate [12]. However, these recommendations are primarily focused on healthy people. Considering that our patients had prostatopathies, and urological diseases themselves can cause vit. D deficiency [13], we divided the examined men according to previously existing guidelines into individuals with sufficient blood vitamin D levels (≥ 30.0 ng/mL) and patients with D-hypovitaminosis (< 30.0 ng/mL) [14]. At the same time, both patients with CP and patients with BPH in groups with different levels of vit. D in the blood had identical BMI values compared to the corresponding controls (Tables 1 and 2).

Analyzing the content of sex hormones in the blood serum, it was found that in patients with CP, the average values of the T level were significantly lower compared to the control. However, in individuals with D-hypovitaminosis, they were significantly lower compared to individuals with sufficient levels of D-hormone in the blood (see Table 1). This was also accompanied by a decrease in the average values of the T/E_2 ratio, which is an indicator of relative androgenization [15] in men with D-hypovitaminosis. At the same time, the levels of vit. D did not significantly affect the content of E_2 in the blood in patients with CP, whose average levels were significantly higher than in men in the control group (see Table 1).

A similar trend in changes in mean T levels and T/E_2 ratios was also observed in patients with BPH, where they were significantly reduced in the presence of D-hypovitaminosis (see Table 2). Meanwhile, mean E_2 values in men with normal vitamin D levels were similar to control group.

All this confirms the data from the literature, as well as our previous studies, which indicate that the content of vit. D in the blood can affect the levels of sex hormones in the blood [7, 8, 16]. In addition, there may be a positive correlation between the levels of vit. D and T in the blood in BPH [17]. However, the correlation analysis did not reveal any relationship between the levels of T and vit. D in either patients with CP and BPH ($r = 0.093$; $P > 0.05$; $r = 0.165$; $P > 0.05$).

Table 1

Levels of vitamin D, hormonal status and sperm parameters in men with chronic prostatitis, ($\bar{X} \pm S_{\bar{X}}$)

Parameter	Group		
	Men with normal vitamin D levels, n = 14	Men with D-hypovitaminosis, n = 18	Control, n = 15
Age, years	31.3 ± 0.8	30.2 ± 0.5	30.0 ± 0.6
BMI, kg/m²	25.2 ± 1.0	26.3 ± 0.6	25.7 ± 0.9
Vitamin D, ng/mL	32.9 ± 1.6	18.5 ± 1.2[1)2)]	33.2 ± 1.7
Testosterone, nmol/L	16.5 ± 0.9[1)]	13.8 ± 0.5[1)2)]	19.8 ± 0.7
Estradiol, nmol/L	0.19 ± 0.01[1)]	0.21 ± 0.01[1)]	0.15 ± 0.01
Testosterone/Estradiol ratio, CU	85.2 ± 4.7[1)]	64.5 ± 3.4[1)2)]	128.5 ± 6.3
Ejaculate volume, mL	3.0 ± 0.2	2.9 ± 0.2	3.1 ± 0.3
Sperm count, million/mL	33.9 ± 2.1[1)]	30.2 ± 1.7[1)]	58.4 ± 3.1
Motile sperm forms, %	37.9 ± 2.1[1)]	30.5 ± 1.2[1)2)]	69.5 ± 3.2
Progressively motile sperm forms, %	20.1 ± 1.2[1)]	14.7 ± 0.9[1)2)]	45.5 ± 2.8
Pathologically altered sperm forms, %	61.2 ± 3.4[1)]	62.9 ± 3.2[1)]	50.5 ± 2.1

Notes:

[1)] Significance of changes compared to the control group;

[2)] Significance of changes compared to the values in men with vitamin D levels > 30.0 ng/mL ($p < 0.05$).

Table 2

Parameters of functional state of testicles, vitamin D levels, hormonal status in men with benign prostatic hyperplasia, ($\bar{X} \pm S_{\bar{X}}$)

Parameter	Group		
	Men with normal vitamin D levels, n = 14	Men with D-hypovitaminosis, n = 17	Control, n = 12
Age, years	40.1 ± 0.7	40.5 ± 0.6	39.8 ± 0.9
BMI, kg/m²	26.8 ± 1.1	25.9 ± 0.9	25.7 ± 1.3
Vitamin D, ng/mL	32.9 ± 1.1	20.3 ± 0.7[1)2)]	34.2 ± 1.2
Testosterone, nmol/L	16.1 ± 0.8	12.6 ± 0.3[1)2)]	17.6 ± 0.5
Estradiol, nmol/L	0.17 ± 0.01	0.20 ± 0.01[1)2)]	0.16 ± 0.01
Testosterone/Estradiol ratio, CU	93.9 ± 5.7	62.8 ± 4.5[1)2)]	110.9 ± 8.3
Ejaculate volume, mL	2.9 ± 0.2[1)]	2.8 ± 0.2	3.1 ± 0.3
Sperm count, million/mL	38.4 ± 2.2[1)]	36.9 ± 2.1[1)]	54.7 ± 3.1
Motile sperm forms, %	46.7 ± 1.1[1)]	35.1 ± 1.0[1)2)]	72.4 ± 3.4
Progressively motile sperm forms, %	28.7 ± 1.6[1)]	20.4 ± 1.5[1)2)]	56.2 ± 3.7
Pathologically altered sperm forms, %	63.5 ± 2.1	70.1 ± 1.2	61.3 ± 2.2

Notes:

[1)] Significance of changes compared to the control group ($p<0.05$);

[2)] Significance of changes compared to the values in men with vitamin D levels > 30.0 ng/mL ($p < 0.05$).

Table 3

Frequency of androgen deficiency in men with prostatopathy depending on the level of vitamin D in the blood, n, %

Group	Level of vitamin D ≥ 30.0 ng/mL		Level of vitamin D < 30.0 ng/mL		Statistical measure	
	Normal Testosterone level	Testosterone is reduced < 12.0 pmol/L	Normal Testosterone level	Testosterone is reduced < 12.0 pmol/L	χ^2	p
Chronic prostatitis n = 32	10 (31.25)	4 (12.50)	8 (25.0)	10 (31.25)	1.36	> 0.05
Benign prostatic hyperplasia n = 31	12 (38.71)	2 (6.45)	7 (22.58)	10 (32.26)	4.68	< 0.05

It should be noted that according to the existing recommendations for the diagnosis of hypogonadism in men [18], none of the patients with CP and BPH had hypogonadal T levels. Meanwhile, an analysis of the frequency of finding the so-called «gray zone» of T levels in the blood, when it is below 12.0 nmol/L but does not reach hypogonadal values [15], indicated its increase in patients with BPH (Table 3).

If the free T content in the blood is not within the normal range, this may indicate the presence of androgen deficiency [15]. Considering that all men in both control groups had a T level in the blood greater than 12.0 nmol/L, it can be stated that in individuals with BPH, D-hypovitaminosis is associated with moderate androgen deficiency.

Infertile men with both CP and BPH, a significant decrease in sperm concentration and motility was observed compared to control values (see Tables 1 and 2). However, under conditions of D-hypovitaminosis, the average values of sperm motility were significantly lower compared to individuals with normal blood levels of vit. D. These data are consistent with the literature, which indicates thatinfertile men, vit. D levels are significantly lower compared to healthy men [5, 7], and vit. D deficiency can lead to deterioration of sperm parameters [6, 16]. This may be due to the decrease in androgenization levels in D-hypovitaminosis that we have established. In addition, vit. D has inherent anti-inflammatory and antioxidant properties [6, 17], the reduction of which in D-hypovitaminosis can negatively affect the state of spermatogenic function in men, which is impaired in pathological conditions in the pancreas [1, 2, 19].

It should also be noted that, unlike some authors who established a correlation between the content of vitamin D and the number of sperm, as well as the number of their motile forms, our study found no such correlation in either patients with CP ($r = 0.223$; $P > 0.05$; $r = 0.182$; $P > 0.05$) or men with BPH ($r = 0.095$; $P > 0.05$; $r = 0.104$; $P > 0.05$).

Thus, summarizing the obtained data, it can be stated that under conditions of D-hypovitaminosis in individuals with CP and BPH, the functional state of the testicles is significantly reduced compared to men with prostatopathy, whose vitamin D levels correspond to or exceed 30.0 ng/mL. In our opinion, this constitutes a rationale for the prescription of cholecalciferol in comprehensive treatment regimens for reproductive dysfunction in young men with CP and BPH and low blood levels of vitamin D.

CONCLUSIONS

1. In infertile men with chronic prostatitis or signs of benign prostatic hyperplasia, under conditions of D-hypovitaminosis, there is a significant decrease in androgenization levels compared to patients in whom the content of vitamin D in the blood is normal.
2. The presence of D-hypovitaminosis in infertile men with chronic prostatitis and benign prostatic hyperplasia significantly affects sperm motility and does not change them.
3. In infertility in men with chronic prostatitis or benign prostatic hyperplasia, there is no correlation between the level of vitamin D and the content of testosterone in the blood, nor with sperm concentration and motility.

REFERENCES

1. Lisovyj VM, Arkatov AV, Knigavko OV. Choloviche bezpliddja: etiopatogenez, diagnostyka, likuvannja, *Kharkiv*, 2011: 128 p.
2. Graziani A, Grande G, Martin M, et al. *Life (Basel)* 2023;13(8): 1700. https://doi.org/10.3390/life 13081/700
3. Motrich DR, Salasar FC, Bleser ML, et al. *Andrologia* 2018;50: e13093. https://doi.org/10.1111/and.13093
4. Madersbacher S, Sampson N, Culig Z. *Gerontology* 2019; 65(5): 458-464. https://doi.org/10.1159/000496289
5. Rehman R, Lalanis, Baig M, et al. *Front Endocrinol* 2018;9: 607. https:/doi.org/10.3389/fendo.2018.00607
6. Brown D, Gzeka K, Narayan Y, et. al. *Longhua Chinese Medicine* 2022; 5(6): 1-10. https://doi.org/10.21037/lcm-21-49
7. Bondarenko VO, Minuhin AS, Skornjakov JI. *Probl Endocrine Pathol* 2021;1: 21-25. https://doi.org/10.21856/j–PEP.2021.1.03
8. Abu-Zaid A, Salen SA, Adly HM, et al. *Descases* 2024; 12(10): 228. https://doi.org/10.3390/diseases12100228
9. Marakhovskyi I O, Laryanovska YB, Korenieva YM, et al. *Rep Morphol* 2022;28(2): 25-31. https://doi.org/10.31393/morphology-journal-2022-28(2)-04
10. Yeo JK, Park SG, Park MG. *World J Mens Health* 2023; 41(4): 874-981. https://doi.org/10.5534/Wjmh. 220180
11. Marakhovskyi IO, Smolienko NP, Korenieva YM, et al. *Rep Morphol* 2024;30(3): 63-79. https://doi.org/10.31393/morphology-journal-2024-30(3)-07
12. Demay MB, Pittas AG, Bikle DD, et al. *J Clin Endocrinol Metab* 2024;109(8): 1907-1947. https://doi.org/10. 1210/clinem/agae 290
13. Lapau WB, Lanrent MR, Rozenberg S, et al. *Nutrients* 2024;16(15): 2388. https://doi.org/10.3390/nu161552388
14. Holic MF, Bincley NC, Bischoff-Ferrasi HA, et al. *J Clin Endocrinol Metab* 2011;96(7): 1911-1930. https://doi.org/10.1210/jc.2011-0385
15. Luchyckyi EV, Bondarenko VA. Izbrannye lekcii po klinicheskoj andrologii, *Kyiv ; Kharkiv*, 2010: 144 p.
16. Bondarenko VO, Goncharova OA, Minuhin AS, Skornjakov JI. *Probl Endocrine Pathol* 2021;3: 31-36. https://doi.org/10.21856/j-PEP.2021.3.04
17. Park SG, Yeo JK, Cho DY, Park MG. *The Aging Male* 2018;21(1): 55-59. https://doi.org/10.1080/13685538.2017.1311857
18. Brasin S, Brito JP, Cunningam GR, et al. *J Clin Endocrinol Metab* 2018;103(5): 1715-1744. https://doi.org/ 10.1210/jc.2018-00229
19. Korenieva Ye, Bondarenko VO, Brechka NM, et al. *Probl Endocrine Pathol* 2023;80(4): 56-65. https://doi.org/10.21856/j-PEP.2023.4.07

FUNCTIONAL STATE OF TESTICLES AND VITAMIN D LEVELS IN THE BLOOD OF YOUNG MEN WITH PROSTATE DISEASES AND INFERTILITY

V. O. Bondarenko [1], Ye. M. Korenieva [1], Ye. I. Skornyakov [1], N. M. Brechka [1,2], I. O. Bielkina [1], N. P. Smolienko [1], A. S. Minuhin [3]

[1] SI «V. Danilevsky Institute for Endocrine Pathology Problems of the NAMS of Ukraine», Kharkiv, Ukraine;

[2] Private establishment of higher education «Kharkiv institute of medicine and biomedical sciences», Kharkiv, Ukraine;

[3] LLC «Instinct of the Sun», Kharkiv, Ukraine

eugenia_koreneva@i.ua

Background. There is data indicating that the blood content of vitamin D able to influence on the level of androgenization and spermogram parameters in men. Nevertheless, how these indicators change in young men with infertility and prostatopathy depending on the presence or absence of D-hypovitaminosis is unknown.

The purpose of the work: To study the features of changes in spermatogenic and endocrine functions of the testes in men with infertility against the background of chronic prostatitis and benign prostatic hyperplasia depending on the blood level of vitamin D.

Materials and methods. The level of testosterone (T) and estradiol (E2) in the blood were analyzed by enzyme immunoassay method in 63 men aged 24–45 years with infertility and prostatopathy depending on the level of vitamin D in the blood: more or less than 30,0 ng/mL, and spermogram parameters were also determined according to WHO recommendations.

Among the examined of 32 persons had characteristics of chronic prostatitis (CP) and 31 patients had benign prostatic hyperplasia (BPH). Similarly, the hormonal status and spermogram parameters were analyzed in 27 practically healthy men of the same age, who made up the control group.

The material was statistically processed by calculating the arithmetic average indica-tors and its deviations ($\bar{X} \pm S_{\bar{X}}$), $\chi 2$ values and Pearson correlation coefficients.

Results. Infertile men with both CP and BPH in the presence of D-hypovitaminosis had significantly reduced averange levels T and T/E2 values compared to individuals whose blood vitamin D levels exceeded 30.0 ng/mL.

At the same time low blood levels of vitamin D in patients with BPH are associated with moderate androgen deficiency, when the content of T in the blood is less than 2.0 nmol/L, but exceeds 9.2 nmol/L, or the limit below which the hypogonadal androgen level is determined. ($\chi 2 = 4.68$; $p < 0.05$).

These changes in androgenization were accompanied by a more significant decrease in the number of motile sperm forms in both groups of patients with D-hypovitaminosis. There is no correlation between the content of vitamin D and blood levels of T, as well as between the level of vitamin D and the number of sperm and their motile forms.

Conclusions. In infertile men with chronic prostatitis or signs of benign prostatic hyperplasia, under conditions of D-hypovitaminosis, there is a significant decrease in androgenization levels compared to patients in whom the content of vitamin D in the blood is normal. The presence of D-hypovitaminosis in infertile men with chronic prostatitis and benign prostatic hyperplasia significantly affects sperm motility and does not change them. In infertility in men with chronic prostatitis or benign prostatic hyperplasia, there is no correlation between the level of vitamin D and the content of testosterone in the blood, nor with sperm concentration and motility.

Keywords: vitamin D, benign prostatic hyperplasia, estradiol, spermogram parameters, testosterone, chronic prostatitis.

ФУНКЦІОНАЛЬНИЙ СТАН СІМ'ЯНИКІВ ТА РІВЕНЬ ВІТАМІНУ D В КРОВІ У ЧОЛОВІКІВ МОЛОДОГО ВІКУ З ПРОСТАТОПАТІЯМИ ТА НЕПЛІДНІСТЮ

Бондаренко В. О.[1], Коренєва Є. М[1]., Скорняков Є. І.[1], Бречка Н. М.[1,2], Бєлкіна І. О.[1], Смолєнко Н. П.[1], Мінухін А. С.[3]

[1] ДУ «Інститут проблем ендокринної патології ім. В. Я. Данилевського НАМН України», м. Харків, Україна;

[2] Приватний заклад вищої освіти «Харківський інститут медицини та біомедичних наук», м. Харків, Україна;

[3] ТОВ «Інстинкт Сонця», м. Харків, Україна

eugenia_koreneva@i.ua

Існують дані, які свідчать, що вміст вітаміну D в крові може впливати на рівень андрогенізації та параметри спермограм у чоловіків. Однак, як ці показники змінюються залежно від наявності та відсутності D-гіповітамінозу у чоловіків молодого віку з неплідністю та простатопатіями не відомо.

Мета роботи: Дослідити особливості змін сперматогенної та інкреторної функцій сім'яників у чоловіків з неплідністю на тлі хронічного простатиту та доброякісної гіперплазії передміхурової залози в залежності від рівня вітаміну D в крові.

Матеріали та методи. Проаналізовано рівні тестостерону (Т) та естрадіолу (E_2) в крові, які визначались імуноферментним методом, а також параметри спермограм згідно з рекомендаціями ВООЗ у 63 чоловіків віком 24–45 років із неплідністю в шлюбі та простатопатіями в залежності від рівня вітаміну D в крові: більше або менше ніж 30,0 нг/мл. Серед обстежених у 32 осіб були ознаки хронічного простатиту (ХП) та у 31 пацієнта – доброякісної гіперплазії передміхурової залози (ДГПЗ). Аналогічно аналізувався гормональний статус і параметри спермограм у 27 практично здорових чоловіків того ж віку, що склали групи контролю. Матеріал оброблено статистично з обчисленням середнього арифметичного та його похибки ($\bar{X} \pm S_{\bar{X}}$), величин χ^2 та коефіцієнтів кореляції Пірсона.

Результати. У неплідних чоловіків як із ХП, так і ДГПЗ за наявності D-гіповітамінозу середні значення рівня Т та величин T/E_2 були суттєво знижені порівняно з особами, у яких вміст вітаміну D в крові перевищував 30,0 нг/мл. При цьому низькі рівні вітаміну D в крові у хворих на ДГПЗ асоційовані з помірним андрогенодефіцитом, коли вміст Т в крові менше ніж 2,0 нмоль/л, але перевищує 9,2 нмоль/л, або межу нижчу за якої визначається гіпогонадний рівень андрогену ($\chi^2 = 4,68$; $p < 0,05$). Дані зміни андрогенізації супроводжувались більш значним зниженням кількості рухливих форм сперміїв в обох групах пацієнтів із D-гіповітамінозом. Не встановлено корелятивної залежності між вмістом вітаміну D та Т в крові, а також між рівнем вітаміну D та кількістю сперміїв та їх рухливих форм.

Висновки. У неплідних чоловіків, хворих на хронічний простатит або з ознаками доброякісної гіперплазії передміхурової залози за умов D-гіповітамінозу існує суттєве зниження рівнів андрогенізації порівняно з хворими, у яких вміст вітаміну D в крові відповідає нормі. Наявність D-гіповітамінозу у неплідних чоловіків з хронічним простатитом та доброякісною гіперплазією передміхурової залози значно впливає на рухливість сперміїв та не змінює їхню концентрацію. При неплідності у чоловіків із хронічним простатитом та доброякісною гіперплазією передміхурової залози відсутня корелятивна залежність між рівнем вітаміну D та вмістом тестостерону в крові, а також із показниками концентрації та рухливості сперміїв.

Ключові слова: вітамін D, доброякісна гіперплазія простати, естрадіол, параметри спермограм, тестостерон, хронічний простатит.