

STRESS AND REPRODUCTIVE DISORDERS: MODERN VIEWS ON THE PROBLEM AND OWN RESEARCH EXPERIENCE*

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Nowadays, the reproductive health of the Ukrainian population is one of the most urgent not only medical but also social problems at the present: now the number of infertile married couples registered in our country is more than 820 thousand [1]. The cause of infertility in marriage in 50 % of cases is reproductive disorders by men [2, 3], which manifest themselves, among other things, in the decrease of sperm quality and quantity [4, 5]. Similar facts have been identified in the selection of donors for the creation of sperm banks [6]: only 10 % of male-sponsored sperm was fit for artificial insemination; more than 85 % of the examined men had stable changes in sperm parameters [7].

According to the literature [8–10], one of the main reasons for the deterioration of the quality of sperm, and hence the decline in fertility, is the negative impact of environmental,

social and/or occupational stress factors on modern men. As known, the sexual function is very sensitive to stress factors, so under their influence, both reproductive and copulative components are changed. Long-term stress can be the cause of sexual disturbances and infertility. One of the main factors that suppress spermatogenesis due to stress include the emergence of a number of hormonal alteration — the decrease in the circulating level of testosterone, dihydrotestosterone, follicle stimulating and luteinizing hormone while increasing the concentration of corticosteroids, prolactin, the predominance of estrogen content over androgens [7, 11].

Such hormonal changes cause a decrease in the effectiveness of protective mechanisms against the effects of damaging factors, primarily of peroxidation products, on the struc-

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ture of reproductive organs. As far as is known, another important pathogenetic factor in the development of male infertility due to stress is the presence of oxidative stress, whose action is primarily manifested in the development of pathospermia. It has now been proved that for the pathospermia there is a negative correlation between the intensity of the PLL processes and the sperm motility and positive — with the number of abnormal forms of sperm [12]. All of this things, should be taken into account in the treatment of infertility caused by stress.

Research of reproductive disorders under the influence of various stress factors — for several decades, one of the main directions of scientific research of the SI «V. Danilevsky Institute for Endocrine Pathology Problems of the NAMS of Ukraine». In the early 90's of the 20th century, under the guidance of Professor Gladkova A. I., the first at that time was started, due to which various aspects of the pathogenesis of reproductive diseases caused by stress were detailed. It has been shown that the manifestations of stress for reproductive function depend on the stage of stress, the type of stressor, they can be detected directly during stress and/or in the long term. It was shown the importance of not only the stress of this person, but also her father [13].

An important result of the Institute's research was the creation of an original pharmacological drug, which has had the ability to positively influence the various pathogenesis of reproductive disorders arising due to stress, without affecting the hormonal status of the organism.

The impetus for such a drug was the fact that modern therapies of infertility in men are mainly due to the use of hormones (gonadotropins, androgens, estrogens) and anti-hormonal drugs. It is known, their reception very often leads to a number of negative complications, in particular, the blocking of gonadotropic function, and because of this, the appearance of sperm cells damaged in quantitative and qualitative terms.

One should also bear in mind the economic component of treatment. Industrial synthesis of hormonal drugs is multistage and expensive, which is reflected in their prices in pharmacy networks. Due to the current difficult economic

situation in our country there is a fairly large number of people who, due to lack of funds, are not able to carry on long-term treatment with such drugs.

The list of the medicines of non-hormonal nature is still extremely limited. As auxiliary drugs for the treatment of male infertility, phytopreparations are used; vitamin therapy, prostaglandins; preparations containing zinc, selenium, essential amino acids, primarily arginine [14].

The main disadvantage of such medicines is the difficulty of dosing in the application, the duration of treatment and not always sufficient efficiency.

Therefore, the specialists of the SI «V. Danilevsky Institute for Endocrine Pathology Problems of the NAMS of Ukraine» synthesized a new original compound, which is 3-N-(4,5-dihydrothiazol-2-yl)amide IR, S, 2S, R-1,2,2-trimethylcyclopentane 1,3-dicarboxylic acid is called Katiazin (KTZ).

The basis for the development of this compound were numerous data on the important role of dicarboxylic acids in a number of biochemical processes, in particular in the gonads and prostate gland [15, 16].

A number of studies have been carried out to determine the mechanisms of action of this original combination and its safety, and to compare its efficacy with regard to various manifestations of male reproductive disorders that arise from stress with existing drugs. It was determined that KTZ does not possess direct estrogenic, antiestrogens, androgenic-anabolic properties, nor does it possess gonadotropic activity.

At the same time, in the conditions of KTZ introduction to animals subjected to immobilization stress, there is a tendency to increase the level of circulating testosterone. Changes in the level of estradiol had an opposite orientation, which led to the normalization of the ratio of sex hormones [17, 18].

The purpose of the study, the results of which were presented in this article, was to compare the effect of KTZ with the action of arginine hydrochloride on the parameters of spermogram and morphometric analysis of the histological structure of the respiratory tract of animals exposed to stress.

MATERIALS AND METHODS

The work was performed on sexually mature 6-month males in rats of the Wistar population with a body weight of 220–300 g. The research was conducted in accordance with the national «General ethical principles of experiments on animals» (Ukraine, 2001), which comply with the provisions of the «European Convention for the Protection of Vertebrate Animals Used for experimental and other scientific purposes» (Strasbourg, 1985). To simulate the pathology of spermatogenesis, animals were stressed for seven days by daily one-hour immobilization on the back with fixation of both pairs of paws, which is a non-physiological state for this species of animals. In accordance with literature [18, 19], rigorous immobilization is considered as sufficiently strong stress and, according to our preliminary data, cause significant damage in reproductive function [20].

Prescribe the KTZ was performed from the first hour of the male's exposure at a dose of 0.6 mg/kg of body weight daily for 21 days intragastrically with a probe, and prescribe the arginine hydrochloride — in a dose of 100 mg/kg body weight.

The control and experimental animals were decapitated, withdrawn and weighed organs of the reproductive system, adrenal glands, thymus and pituitary gland.

Generative function of males was estimated by the indicators of spermogram and morpho-

metric analysis of the histological structure of the testicles. The concentration of sperm, their mobility and the number of pathological forms according to the generally accepted method was determined. For morphological studies, the testes were fixed in 10 % formalin. Coloring was carried out using hematoxylin and eosin according to generally accepted methods.

The index of spermatogenesis, the diameter of the spermatid tubules, the number of cells of the initial stage of spermatogenesis (spermatogonia), which are important criteria for predicting fertility, were evaluated using histological sections. To calculate the index of spermatogenesis, 100 seminal tubules were reviewed, each of which was evaluated by a four-point system. The diameter of the channel sections of the rounded section was measured using an ocular micrometer with an increase of $\times 400$.

Received data was statistically analyzed. The normality of the distribution of variables was determined using the Kolmogorov-Smirnov test. Since the indicators responded to the law of normal distribution, the data in the tables are presented as mean and standard error of mean ($X \pm S_x$). The multiple comparisons between the control and the following groups were performed using a one-factor dispersion analysis. A probability (p) value of 5 % or less was considered statistically significant ($p < 0,05$).

RESULTS AND THEIR DISCUSSION

After seven days of stress, the body weight of the experimental rats was reduced compared to intact animals. At the same time, the relative weight of their adrenal glands, pituitary gland and thymus increased by 27 %, 33 % and 52 %, respectively, relative to untreated rats (Table 1). The obtained data may indicate a violation of the function of the above-mentioned organs in stress, which is confirmed by the data of literature [21], that is, on the effective modeling of stress and the hormonal disorders caused by it.

In animals taking KTZ, there was an increase in the mass of only one of the main stress-related organs — the adrenal glands, which indirectly can testify to the positive effect of KTZ on hormonal regulation processes.

But this statement needs to be studied in detail in the process of further research.

Regarding to androgen-dependent organs, there was an increase in only the weight of the testicles, while the relative weight of the prostate gland was slightly lower than normal. This may be explained by an increase in the sexual activity of these animals.

At the next stage of work, it was confirmed that stress affects negatively the indicators of spermogram. The largest pathological changes are the parameter «concentration of sperm», which is reduced by almost 3 times in comparison with the group of intact animals, with simultaneous decrease in mobility and an increase in the percentage of pathological forms almost 2 times.

Table 1

Relative mass of androgen-responsive organs of male rats

Indicator	Group		
	Intact, n = 10	Stress, n = 10	Stress + KTZ, n = 5
Body weight, g	298.9 ± 4.6	264.4 ± 5.7*	275.0 ± 15.1
Testes, mg/100 g	971.8 ± 56.1	981.8 ± 65.5	1200.0 ± 30.5*/**
Epididymisy, mg/100 g	327.8 ± 16.9	309.1 ± 24.3	370.3 ± 13.6**
Seminal vesicles, mg/100 g	235.5 ± 15.9	218.3 ± 8.2	331.6 ± 14.0**
Prostate, mg/100 g	295.6 ± 8.2	244.5 ± 15.7*	171.2 ± 20.1*/**
Adrenal glands, mg/100 g	13.9 ± 0.7	17.7 ± 0.8*	19.6 ± 1.6*
Thymus, mg/100 g	35.3 ± 3.3	53.9 ± 4.1*	39.5 ± 2.9**
Pituitary, mg/100 g	2.7 ± 0.2	3.6 ± 0.1*	2.9 ± 0.3**

Notes:

* — statistically significant differences in comparison with the data for the Intact group, $p \leq 0.05$;

** — statistically significant differences in comparison with the data for the Stress group, $p \leq 0.05$.

Subsequently, in the course of work, it was determined that all the animals that received intrauterine tissue injections, in comparison with the spermogram of stressed rats, improved all the parameters of the spermogram: the concentration ($p < 0.05$) and sperm motility ($p < 0.05$), the number of their pathological forms decreased ($p < 0.05$) (Table 2).

The results of the comparative analysis indicate that the positive effect of KTZ is expressed to a greater extent than the effect of arginine in similar conditions (Table 2).

However, it is noteworthy that neither KTZ nor arginine hydrochloride reduced the number of morphologically abnormal germ cells to the level of the intact group increased as a result of male males.

After confirmation of the effectiveness of the KTZ in improving the characteristics of spermograms it became necessary to establish its place in the process of gametes formation, and for this morphometric studies have been performed. The results obtained are presented in Table 3.

Table 2

Correction of spermatogenic function of male rats

Group, number of animals	Sperm		
	concentration, ml/ml	motility, %	pathological forms, %
Intact, n = 13	47.6 ± 4.5	74.4 ± 1.2	28.31 ± 3.2
Stress, n = 5	17.6 ± 0.6*	38.8 ± 2.1*	57.0 ± 4.6*
Stress + KTZ, n = 8	28.8 ± 1.8*/**/**	71.8 ± 2.5**/**	42.3 ± 3.6*/**
Stress + arginine hydrochloride, n=6	19.8 ± 1.7*/**	60.8 ± 4.6*/**	52.7 ± 5.5*

Notes:

* — statistically significant differences in comparison with the data for the Intact group, $p \leq 0.05$;

** — statistically significant differences in comparison with the data for the Stress group, $p \leq 0.05$;

*** — statistically significant differences in comparison with the data for the group «Stress + arginine hydrochloride», $p \leq 0.05$.

Morphometric parameters testes of male rats that received the experimental therapy

Group	Diameter of tubules, conditional units, n = 60	Number of spermatogonia, pcs., n = 30	Spermatogenesis index, score, n = 100
Intact	67.48 ± 1.1	86.60 ± 2.7	3.58 ± 0.04
Stress	58.69 ± 1.5*	76.90 ± 3.6*	3.06 ± 0.05*
Stress + KTZ	63.07 ± 1.2*/**	91.87 ± 2.9**	3.45 ± 0.10**

Notes:

* — statistically significant differences in comparison with the data for the Intact group, $p \leq 0.05$;

** — statistically significant differences in comparison with the data for the Stress group, $p \leq 0.05$.

It should be noted that all morphometric indices of the testes of stressed rats were significantly worsened relative to the intact group, at the level $p \leq 0.05$: the diameter of the tubules 1.2 times; the number of spermatozoa in 1.1 times; The index of spermatogenesis in 1.2 times. But in animals treated with KTZ, we observed an increase in the diameter of the spermatid tubules and the presentation of the number of spermatogonia and the index of spermatogenesis to the level of the intact group (see Table 3).

Consequently, summing up all the above, it becomes clear that all indications for the appointment of the KTZ are all forms of spermatogenesis disorders, among which the greatest effectiveness is determined with respect to the mobility of sperm, and other indicators are changing in the following sequence: increasing the concentration of spermatozoa > reducing the number of pathological forms.

Under the influence of KTZ, the formation of germ cells is activated both at the stage of maturation of the sperm from the spermatid, and at the stage of formation of spermatogonia. These data substantiate the possibility of using KTZ for the treatment and prevention of sperm motility disorders.

A promising direction for further research is the assessment of the effect of this drug on

the development of insulin resistance and associated metabolic disorders. Thus, according to literature, these factors significantly impair male reproductive function under the influence of stress of different nature [22].

The results of the effects of arginine hydrochloride and KTZ comparison, which are highlighted above, give an optimistic result regarding to the endothelium protective effect of the latter [23], which causes the work in this direction.

Given the literature data on the leading role of lipid peroxidation in the development of reproductive disorders in stress, there is a need for a detailed study that would determine the effect of this compound on the system of lipid peroxidation and antioxidant protection, namely on the activity of antioxidant enzymes (catalase, glutathione peroxidase, glutathione-S-transferase) and the content of reduced glutathione in semen and seminal plasma; activity of superoxide dismutase [12].

But the analysis of results, which have already obtained, allow us to suppose the specific effect of the experimental drug called KTZ. The results obtained by us show the high efficiency of KTZ in the treatment of male infertility, namely, for the treatment of spermatogenesis disturbance.

CONCLUSIONS

1. The compound called Katiazin has the properties of improving the parameters of spermatogenesis in rats with impaired cellular cycle of sperm formation, which arose as a result of their stress.
2. Taking the Katiazin leads to the activation of the germ cells formation at all stages of spermatogenesis.
3. Taking the Katiazin is more effective compared to arginine hydrochloride in order

to improve spermograms such as «concentration and sperm motility», morphometric characteristics of the testicles.

4. A biologically active compound Katiazin might be recommended for further clinical trials in men with stress-induced pathospermia.

ЛИТЕРАТУРА (REFERENCES)

- Serdjuk AM, Kundijev JuI, Nagorna AM, Shyrobokov VP. *Zhurn NAMN Ukrainy* 2012; 18 (3): 358-371.
- Morin SJ, Scott RT *Transl Androl Urol* 2018; 7 (3): S283-S291. doi: 10.21037/tau.2018.05.02.
- Santi D, De Vincentis S, Magnani E, Spaggiari G. *Andrology* 2017; 5 (4): 695-703. doi: 10.1111/andr.12379.
- Sengupta P, Borges EJr, Dutta S, Krajewska-Kulak E. *Hum Exp Toxicol* 2018; 37 (3): 247-255. doi: 10.1177/0960327117703690.
- Levine H, Jørgensen N, Martino-Andrade A, et al. *Hum Reprod Update* 2017; 23: 646-659. doi: 10.1093/humupd/dmx022.
- Volkova NO, Juhta MS, Chernishenko LG, et al. *Problemy Kriobiologii i Kriomediciny* 2017; 27 (3): 203-218.
- Nikiforov OA, Avramenko NV, Lomejko EA, Bachurin GV. *Aktual'nye voprosy farmacevticheskoy i medicinskoj nauki i praktiki* 2015; 3 (19): 76-80.
- Knez J. *Reprod Biomed Online* 2013; 26: 440-448. doi: 10.1016/j.rbmo.2013.02.005.
- Bonde JP. *Curr Opin Endocrinol Diabetes Obes* 2013; 20: 234-239. doi: 10.1097/MED.0b013e32835f3d4b.
- Sharma R, Biedenharn KR, Fedor JM, Agarwal A. *Reprod Biol Endocrinol* 2013;11: 66. doi: 10.1186/1477-7827-11-66.
- Ren L, Li X, Weng Q, et al. *J Vet Med Sci* 2010; 72: 1501-1506.
- Bykova MV. Narushenie redoks-balansa spermatozoidov i semennoj plazmy muzhchin pri patospermii, *Krasnojarsk*, 2008: 24 p.
- Chystjakova EJe, Gladkova AI. *Probl Endokryn Patologii'* 2008; 4: 84-91.
- Gorpynchenko II, Romanjuk MG. *Zdorov'e Muzhchiny* 2016; 1 (56): 8-17.
- Patent 38130A. 3-(4,5-Dygidrotiazol-2-il)amid cys-1,2,2-trymetylcyk-lopentan-1,3-dykarbonovoi' kysloty, shho stymuljuje spermatogenez.
- Zolotuhyna VM, Nykytchenko JuV, Jaremenko FG, Zolotuhyna AA. Nauka i social'ni problemy suspil'stva: medycyna, farmacija, biotehnologija: Tez. Dop, *Harkiv*, 2003; 2: 82.
- Gladkova AI, Sidorova IV, Jaremenko FG, Zolotuhyna VN. *Probl Endokryn Patologii'* 2012; 4: 102-108.
- Valuskova P, Farar V, Janisova K, et al. *Stress* 2017; 20 (1): 36-43. doi: 10.1080/10253890.2016.1263836.
- Török B, Sipos E, Pivac N, Zelena D. *Prog Neuropsychopharmacol Biol Psychiatry* 2019; 90: 117-133. doi: 10.1016/j.pnpbp.2018.11.013.
- Chistjakova E. E. *Probl Endokryn Patologii'* 2008; 2: 43-49.
- Ren L, Li X, Weng Q, et al. *J Vet Med Sci* 2010; 72: 1501-1506.
- Tjuzikov IA, Kalinchenko SJu, Vorslov LO, Tishova JuA. *Jeksperimental' naja i klinicheskaja urologija* 2014; 2: 68-75.
- Bondarenko VA, Karpenko NA, Velichko NF, et al. *Zdorov'e Muzhchiny* 2014; 1 (48): 142-144.

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MODERN VIEWS ON THE PROBLEM AND OWN RESEARCH EXPERIENCE**

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Modern therapy of infertility in men is mainly associated with the use of hormonal and anti-hormonal drugs, but hormonal therapy often leads to a number of negative complications. The list of non-hormonal nature is extremely limited, which is why the study of effective and safe non-hormonal drugs for the treatment of pathospermia and infertility remains an urgent task.

The purpose of our work was to evaluate the effectiveness of the new biologically active compound Katiazin — a non-hormonal medicine — for the treatment of pathospermia.

The work was performed on sexually mature 6-month rats' males of the Vistar population. To simulate the pathology of spermatogenesis, animals were stressed for seven days by daily one-hour immobilization on the back with fixation of both pairs of paws. The appointment of Katiazin was carried out from the first day of male exertion in a dose of 0.6 mg/kg body weight daily for 21 days intragastrically. Generative function of males was estimated by the indicators of spermogram and morphometric analysis of the histological structure of the testicles.

It was found that stressing of rats affects all the indicators of spermatogenesis, namely, the amount and mobility of spermatozoa decreases and, conversely, the percentage of pathological cells increases. In animals who taking the Katiazin, all the parameters of spermogram of rats were improved. The analysis of morphometric data suggests that the formation of germ cells at the stage of maturation of sperm from the spermatoid and the stage of spermatogenesis is activated under the influence of Katiazin.

The results allow us to recommend Katiazin for the development of a new drug for the treatment of male infertility.

Key words: male infertility, pathospermia, spermatogenesis.

**СТРЕС ТА РЕПРОДУКТИВНІ РОЗЛАДИ:
СУЧАСНІ ПОГЛЯДИ НА ПРОБЛЕМУ ТА ВЛАСНИЙ ДОСВІД ДОСЛІДЖЕНЬ**

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Сучасна терапія безпліддя у чоловіків пов'язана, головним чином, із застосуванням гормональних та антигормональних препаратів, але гормональна терапія нерідко приводить до ряду негативних ускладнень. Перелік засобів негормональної природи вкрай обмежений, саме тому дослідження ефективних і безпечних негормональних засобів для лікування патоспермії і безпліддя залишається актуальним завданням.

Метою нашої роботи було оцінити ефективність нового біологічно активного з'єднання Катіазіна, – негормонального препарату — для лікування патоспермії.

Роботу виконано на статевозрілих 6 місячних самцях щурах популяції Вістар. Для моделювання патології порушення сперматогенної функції тварин стресували протягом семи діб шляхом щоденної одноденної іммобілізації на спині з фіксацією обох пар лап. Призначення Катіазіна здійснювали з першої доби стресування самця у дозі 0,6 мг/кг м. т. щоденно протягом 21 доби внутрішньошлунково. Генеративну функцію самців оцінювали за показниками спермограми та морфометричного аналізу гістологічної будови сім'яників.

Стресування щурів впливає на всі показники сперматогенезу, а саме, зменшується кількість та рухливість сперматозоїдів та навпаки збільшується відсоток патологічних клітин. У тварин які отримували всередину Катіазин поліпшувалися всі показники спермограми щурів. Аналіз морфометричних даних свідчить про те, що під впливом Катіазіна активується утворення статевих клітин як на стадії дозрівання сперматозоїдів із сперматид, так і на стадії утворення сперматогоніїв.

Отримані результати дозволяють рекомендувати з'єднання Катіазин для розробки нового препарату для лікування чоловічого безпліддя.

Ключові слова: чоловіче безпліддя, патоспермія, сперматогенез.

**СТРЕСС И РЕПРОДУКТИВНЫЕ РАССТРОЙСТВА:
СОВРЕМЕННЫЙ ВЗГЛЯД НА ПРОБЛЕМУ
И СОБСТВЕННЫЙ ОПЫТ ИССЛЕДОВАНИЙ**

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Современная терапия бесплодия у мужчин связана, главным образом, с применением гормональных и антигормональных препаратов, но гормональная терапия нередко приводит к ряду негативных осложнений. Выбор средств негормональной природы крайне ограничен, поэтому исследования эффективных и безопасных негормональных средств для лечения патоспермии и бесплодия остается актуальной задачей.

Целью нашей работы было оценить эффективность нового биологически активного соединения Катиазин, — негормональный препарат — для лечения патоспермии.

Работа выполнена на половозрелых 6 месячных самцах крысах популяции Вистар. Для моделирования патологии нарушения сперматогенной функции животных стрессировали в течение семи суток путем ежедневной одночасовой иммобилизации на спине с фиксацией обеих пар лап. Назначение Катиазина осуществляли с первых суток стрессирования самца в дозе 0,6 мг/кг массы тела. Ежедневно в течение 21 суток внутрижелудочно. Генеративную функцию самцов оценивали по показателям спермограммы и морфометрического анализа гистологического строения семенников.

Стрессирование крыс влияет на все показатели сперматогенеза, а именно, уменьшается количество и подвижность сперматозоидов и наоборот увеличивается процент патологических клеток. У животных получавших внутрь Катиазин улучшались все показатели спермограммы. Анализ морфометрических данных свидетельствует о том, что под влиянием Катиазина активируется образование половых клеток как на стадии созревания сперматозоидов из сперматид, так и на стадии образования сперматогоний.

Полученные результаты позволяют рекомендовать соединения Катиазин для разработки нового препарата для лечения мужского бесплодия.

Ключевые слова: мужское бесплодие, патоспермия, сперматогенез.