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Dynamics of Changes IN the Relationship of Hormones of the Reproductive System of Female Rats IN the Post-Intensive Care Period, After Modeling a 10-Minute Clinical Death

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Abstract: Understanding the development of post-intensive care syndrome remains a pressing concern within the field of intensive care worldwide. The stress response triggered by extreme conditions is intricately linked to individual adaptation mechanisms within the autonomous nervous and neuroendocrine systems. Despite this interconnectedness, the impact of post-intensive care on the hormonal dynamics of the reproductive system remains relatively understudied in modern fundamental and clinical medicine. To address this gap, our study aimed to investigate the hormonal fluctuations in the reproductive system of female rats during the post-intensive care period. We conducted experiments on 80 sexually mature female rats, weighing between 160-180g and of mongrel, white descent, using a method pioneered by V.G. Korpachev in 1982 to induce clinical death and simulate post-resuscitation illness. We assessed both the reactivity of the autonomic nervous system and the hormone levels in the reproductive system of the female rats. During the early post-intensive care phase, characterized by a sympathetic nervous system dominance, a compensatory adaptive response was observed. This response facilitated the synthesis and secretion of follicle-stimulating hormone, luteinizing hormone, estradiol, and progesterone. However, in the long-term post-intensive care period, with a further increase in sympathetic nervous system activity, a decline in the levels of these hormones was noted. This downward trend indicated the onset of maladaptation, leading to a depletion of the reproductive system.

Keywords: Clinical death, post-intensive care disease, autonomic nervous system, follicle stimulating hormone, luteinizing hormone, estradiol, progesterone.

Introduction

Numerous scientific investigations are underway globally to enhance the evaluation of reproductive system disorders linked to disruptions in endocrine system reactivity—specifically, disturbances in the interplay among anabolic, catabolic, and kinetic hormones when exposed to diverse extreme stimuli. Presently, the fluctuation patterns in reproductive steroid hormone levels in post-intensive care settings are not well understood. Nonetheless, experimental studies have delineated the morpho-functional changes in the hypothalamic-pituitary system, along with the post-resuscitation protective effects of parenterally administered estrogenic hormones, progesterone, and testosterone.

Literature analysis reveals that while some glands have been examined for endocrine system dysfunctions during post-intensive care disease—such as the hypothalamic-pituitary neurosecretory system, adrenal glands, thyroid gland, and pancreas—the exploration remains partial.

Across the globe, endeavors are underway to establish healthcare systems that radically enhance medical care quality and efficacy for the populace. These efforts encompass early diagnosis, effective treatment, prevention, and complication reduction for various somatic diseases. Against this backdrop, it is advisable to conduct scientific research aimed at appraising disruptions in the female body's

reproductive system during the post-intensive care phase. However, the comprehensive study of alterations in the functional synthesis and secretion of female hormones and their role in adaptation processes during this period remains inadequately explored, presenting a pressing challenge.

The purpose of the study. To ascertain the responsiveness of both the autonomic nervous system and the hormonal profile of the female reproductive system during the post-intensive care period.

The object of the study. In pursuit of this objective, an investigation was carried out involving 80 mongrel female rats weighing between 150-180 g. Among them were 10 intact animals and 70 experimental subjects, wherein the responsiveness of both the autonomic nervous system and the hormones within the reproductive system was examined during clinical death and throughout the post-intensive care phase.

Research Methods

To accomplish the objective and address the challenges associated with clinical death and post-resuscitation illness, the methodology devised by V.G. Korpachev was implemented [8]. The reactivity of the autonomic nervous system was assessed utilizing the Hildebrant coefficient [1], where an elevation in the coefficient signifies a predominance of sympathetic nervous system tone, while a reduction indicates dominance of parasympathetic nervous system tone. Hormonal levels within the reproductive system were determined employing enzyme immunoassay techniques.

Results and Discussion

The examination of autonomic nervous system reactivity and reproductive system hormones in rats during clinical death and the post-resuscitation period revealed the following dynamics of change (refer to Table №. 1).

In intact rats during estrus of the estrous cycle, the Hildebrant coefficient was 5.3±0.04, with follicle-stimulating hormone levels at 14.7±0.9 IU/ml, luteinizing hormone at 43.1±2.3 IU/ml, estradiol at 214.7±11.2 pg/ml, and progesterone at 2.5±0.2 nmol/ml.

During the diestrous period, follicle-stimulating hormone measured 157.6±1.9 IU/ml, luteinizing hormone 17.5±0.5 IU/ml, estradiol 81.8±2.2 pg/ml, and progesterone 9.7±0.3 nmol/ml. Interpreting these findings in conjunction with those of Bain A.M. [1], Kovalev Yu.O. [7], and Karabaeva A.G [16,14], it appears that amidst altered autonomic nervous system reactivity, the hormones of the reproductive system demonstrate moderate functional activity during both estrus and diestrus periods.

During the simulation of 10-minute clinical death in both estrus and diestrus phases, a transient elevation in the Hildebrant coefficient, signifying sympathetic nervous system dominance ($P<0.05$), was observed in autonomic nervous system reactivity. This shift was succeeded by a predominance of parasympathetic nervous system tone, culminating in cardiac arrest. Concurrently, an augmentation in follicle-stimulating hormone, luteinizing hormone, estradiol, and progesterone levels was noted in both groups. However, these changes were statistically insignificant compared to intact animals ($P>0.05$).

In the early post-resuscitation phase, within 24 hours, animals in estrus and diestrus phases exhibited heightened Hildebrant coefficient values indicating sympathetic nervous system dominance ($P<0.001$), along with elevated levels of follicle-stimulating hormone, luteinizing hormone, estradiol, and progesterone compared to intact animals ($P<0.01$).

Table №. 1. Simulation of 10-minute clinical death in both estrus and diestrus phases

The reproductive system during estrus								
Indicators	Intact	10min cl.death	In the post-intensive care period through					
			10 min cl.death	24 hours	15 days	21 days	28 days	58 days
Hildebrant coefficient	5,3± 0,04	5,5± 0,2	6,3± 0,1***	6,0± 0,1*	5,7± 0,2	5,6± 0,1	5,8± 0,1*	5,9± 0,1*

FSH IU/ml	14,7± 0,9	15,8± 0,7	21,4± 0,7**	19,8± 0,7**	18,6± 0,5*	13,8± 0,4	12,1± 0,4*	11,3± 0,5*
LH IU/ml	43,1± 2,3	46,12± 1,1	58,2± 1,7**	53,6± 1,0**	49,1± 0,4*	43,4± 0,8	36,1± 1,4*	34,6± 1,3*
Estradiol pg/ml	214,7± 11,2	227,8± 0,6	281,6± 5,1**	245,6± 2,6*	244,3± 1,3*	210,7± 1,0	181,8± 3,2*	180,2± 3,1*
of progesterone nmol/ml	2,5± 0,2	2,6± 0,2	2,9± 0,1	2,8± 0,1	2,1± 0,1	1,8± 0,2	2,0± 0,1*	1,8± 0,1**
The reproductive system during the period of diestrus								
Indicators	Intact	10 min cl.death	24 hours	15 days	21 days	28 days	58 days	86 days
Hildebrant coefficient	5,3± 0,04	5,5± 0,1	6,2± 0,1***	5,8± 0,1*	5,6± 0,1	5,5± 0,1	5,7± 0,1*	5,8± 0,1*
FSH IU/ml	157,6± 1,9	167,2± 5,0	222,4± 0,7**	207,6± 8,5**	184,1± 7,9*	166,7± 3,8	149,08± 1,7*	143,8± 2,8**
LH IU/ml	17,5±0,5	19,2± 0,3	27± 1,1**	23,1± 0,4***	20,2± 0,7*	18,6± 0,3	15,7± 0,4*	15,3± 0,3**
Estradiol pg/ml	81,8± 2,2	88,2± 1,9	103,8± 5,4**	75,5± 0,4*	72,6± 0,6**	79,4± 1,5	73,5± 1,5*	70,4± 0,7**
of progesterone nmol/ml	9,7± 0,3	9,8± 0,2	24,6± 3,6**	10,9± 0,7	10,1± 0,5	9,7± 0,5	8,5± 0,4*	7,9± 0,1**

**Note: P<0,05-*; P<0,01-*; P<0,001-*;*

After 14 days of revival, no estrus was observed in the animals. On day 15, during both estrus and diestrus phases, a decrease in the Hildebrandt coefficient (P<0.05), indicating reduced sympathetic nervous system reactivity, along with declines in follicle-stimulating hormone, luteinizing hormone, estradiol, and progesterone levels, was noted compared to previous monitoring periods. However, these levels remained elevated compared to intact animals (P<0.01) and (P>0.05).

By the 21st day of post-resuscitation illness, during both estrus and diestrus phases, a decline in the Hildebrant coefficient index was observed, approaching levels seen in intact animals (P>0.05), indicative of a mixed reactivity pattern. Meanwhile, levels of follicle-stimulating hormone, luteinizing hormone, estradiol, and progesterone continued to decrease compared to earlier follow-up periods but remained elevated compared to intact animals (P<0.05). Although progesterone levels were lower compared to intact animals, the differences were insignificant (P>0.05).

In the long-term post-intensive care disease phase, by the 28th day of illness, both groups exhibited a mixed autonomic nervous system reactivity pattern, with declining levels of follicle-stimulating hormone, luteinizing hormone, estradiol, and progesterone compared to intact animals, albeit insignificantly (P>0.05). Additionally, the intervals between cycles continued to lengthen.

By the 58th day of illness, corresponding to the end of the second month, animals displayed an upsurge in the Hildebrandt coefficient—indicating heightened sympathetic nervous system tone—and a further reduction in follicle-stimulating hormone, luteinizing hormone, estradiol, and progesterone levels compared to intact animals (P<0.05). Progressing to the 86th day of illness, amid a continued elevation in the Hildebrandt coefficient—reflecting increased sympathetic nervous system activity—a significant decrease in follicle-stimulating hormone, luteinizing hormone, estradiol, and progesterone levels within the reproductive system was observed compared to intact animals (P<0.01).

During the early post-resuscitation period (refer to Graph № 1), specifically within 24 hours post-recovery, a marked increase in sympathetic nervous system tone was noted during both estrus and diestrus phases. This increase correlated with elevated levels of follicle-stimulating hormone by 1.46 times, luteinizing hormone by 1.4 times, estradiol by 1.31 times, and progesterone by 1.16 times during estrus, and with follicle-stimulating hormone increasing by 1.4 times, luteinizing hormone by 1.54 times, estradiol by 1.27 times, and progesterone by 2.52 times during diestrus compared to intact

animals. Interpreting these findings alongside those of P.D.Horizontov, it appears that hormones crucial for reproductive function participate in the adaptation process during the early post-intensive care phase amidst increased sympathetic nervous system tone [5]. The rise in estradiol concentration in the bloodstream enhances the sensitivity of alpha- and beta-adrenergic receptors to catecholamines, facilitating adaptive processes [9,20].

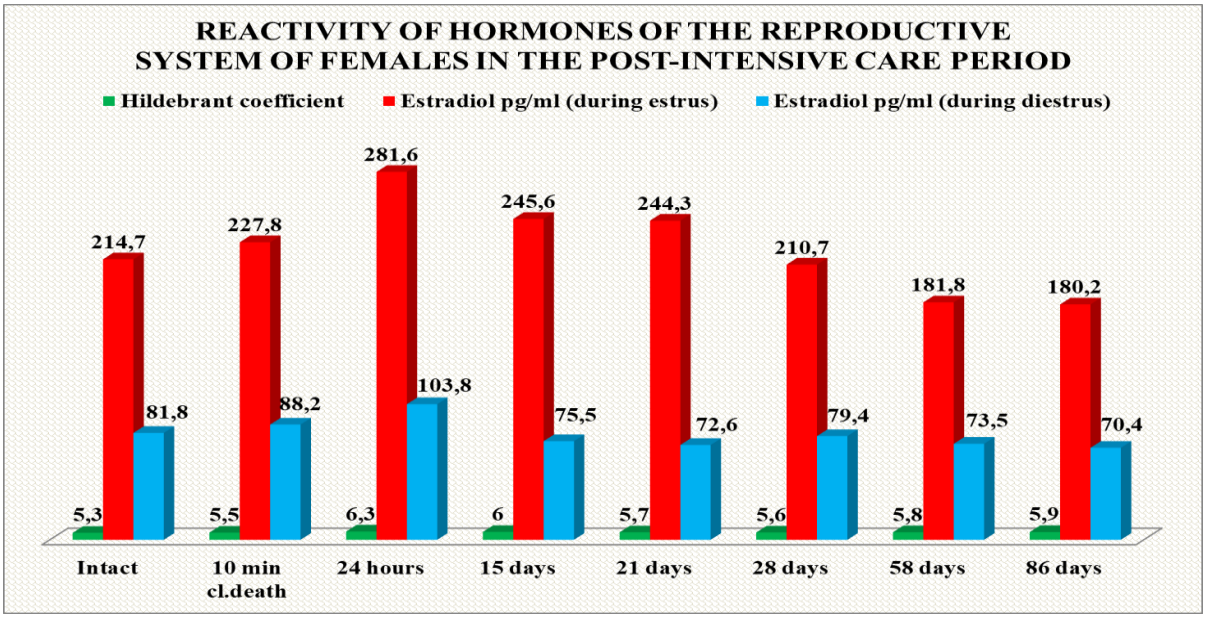

Fig. 1. Reactivity of hormones of the reproductive system of females in the post-intensive care period after modeling a 10-minute clinical death

In the prolonged post-intensive care disease phases during both estrus and diestrus, amid a continued elevation in sympathetic nervous system activity, a decrease in follicle-stimulating hormone levels by 1.1 and 0.8 times, luteinizing hormone levels by 1.14 and 1.23 times, estradiol levels by 1.2 and 0.7 times, and progesterone levels by 1.23 and 0.7 times was observed. Interpreting these findings in conjunction with those of A.G. Karabaev [16], this state signifies the onset of maladaptation with a shift towards depletion in the hormonal structures of the reproductive system.

Conclusion

Based on the gathered data, the following conclusions can be inferred:

- In intact rats, the reproductive system operates at a moderate functional level amidst a mixed autonomic nervous system reactivity.
- During the early post-intensive care phase, the heightened sympathetic nervous system tone leads to increased synthesis and secretion of follicle-stimulating hormone, luteinizing hormone, estradiol, and progesterone, driven by a compensatory adaptive response.
- In the prolonged post-resuscitation illness phase, characterized by heightened sympathetic nervous system activity, a decline in follicle-stimulating hormone, luteinizing hormone, estradiol, and progesterone levels indicates maladaptation, shifting towards depletion of the reproductive system.

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