PREDICTION OF THE RISK OF DEVELOPING SECONDARY EMPTY SELLA SYNDROME

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Abstract. *A prognostic assessment of risk factors for the development of secondary empty sella syndrome with the formation of risk groups was performed using 51 individuals as an example. Risk factors for the development of secondary ESS syndrome include a history of treatment of pituitary micro- and macroadenomas with dopamine agonists, the number of pregnancies up to 3, then in descending order normal body weight, age of patients from 30 to 40 years, men, and headaches.*
Keywords*: pituitary gland, sella turcica, risk factors, integral assessment, likelihood ratio.*

Introduction. Empty sella syndrome (ESS) is a primary failure of the sella diaphragm or failure of the sella turcica that develops after drug, surgical, or radiation treatment of pituitary adenomas, which leads to one of the layers of the dura mater falling into the sella turcica cavity, accumulation of cerebrospinal fluid, compression and flattening of the pituitary gland, stretching of the pituitary stalk, and the development of endocrine, visual, and neurological changes [3,4,8].

It is known that ESS most often affects women (4/5) aged 35 to 55 years [4,5]. Due to the widespread use of magnetic resonance imaging of the brain and the increase in the number of patients undergoing radiation, surgical and combined methods of treatment of patients with pituitary tumors, the diagnosis of the "empty" sella syndrome increases from year to year. At the same time, doctors often consider this syndrome as a radiological finding, since this syndrome does not have specific bright clinical symptoms. Patients go for a long time without being examined and are patients of gynecologists, neurologists and ophthalmologists. The serious complications of ESS are severe endocrine and neurological complications and vision loss. Therefore, each patient with PTSD should be carefully examined and dynamically monitored.

A distinction is made between primary (idiopathic) ESS, secondary ESS, which occurs after radiation, surgical and combined methods of treating diseases of the chiasmatic-sellar region, and developing ESS, which is the initial stage of the general process [1,5,6].

The clinical picture of the disease, except for the symptom of ESS, is nonspecific, but varied. Some patients have no symptoms [2,7]. Another part of patients complains of headaches, dizziness, memory impairment, increased blood pressure (the hypothalamic origin of which is being clarified), changes in vision, endocrine dysfunction depending on the level of hormonal damage, including hyperprolactinemia and hypopituitarism[2,4].

The risk of developing a particular disease is based on establishing a relationship between various factors - indicators (medical and biological, physiological, environmental conditions). These factors, individually and in combination, increase the individual risk of developing the disease.

Forecasting adverse consequences taking into account the complex impact of numerous factors is very relevant, as it allows not only to take into account the degree of probability of such consequences, but also to isolate from the many risk factors those that seem most significant.

The purpose of our research. The purpose of this study was to conduct a prognostic assessment of risk factors (using secondary ESS as an example) to determine the degree of significance of modifying factors in predicting the development of ESS syndrome.

Material and methods of research. The number of examined persons was 51 people, including 40 women and 11 men. The average age of patients was 37.9±0.86 years (37.6±0.93 years for women and 39±2.29 years for men). The comparison group (control group) consisted of persons (38 people)

with forming ESS. The use of these patients as a comparison group is due to the fact that, firstly, this is the initial stage of the process, and secondly, the formation of secondary ESS is most often based on the use of one or another therapy in the treatment of pituitary micro- and macroadenomas, which is completely unacceptable for the general control group of healthy persons.

Using the likelihood ratio method, through an integrated assessment of prognostic criteria, we determined the degree of probability of the effect of its impact on the formation of ESS syndrome, and carried out a prognostic assessment of risk factors.

The complex of assessed factors included: gender, age, body mass index, type of therapy for the disease that led to the formation of secondary ESS (dopaminomimetics, radiation therapy, surgery, combination therapy, Sheehan's syndrome, long-term use of oral contraceptives, thyroid drugs, electrocoagulation of the adrenal artery in Itsenko-Cushing syndrome), gynecological history (number of pregnancies up to 3, more than 3, infertility, no pregnancies), patient complaints (headache, visual impairment, menstrual irregularities, clinical symptoms of hypothyroidism, weight gain), hyperprolactinemia, lactorea, thyroid-stimulating hormone (TSH) level. When developing data for each factor in the main and control groups, likelihood ratios (P main and P control) were calculated and the likelihood ratio (R) was calculated.

Results and discussion. When developing the data, likelihood ratios (P main and P control) were calculated for each factor in the main and control groups. At the next stage, the likelihood ratio (R) was calculated by dividing the likelihood ratio of the main group by the coefficient of the control group.

After calculating R, an integrated assessment of the minimum and maximum degree of possible risk of the development of the phenomenon was carried out.

Below is a prognostic matrix regarding the formation of secondary ESS based on predisposing factors of the probable risk of its development (Table 1).

Calculation of the indicators taken into account made it possible to assess the significance of risk factors and form groups (low, medium, high).

Table 1

Integrated and prognostic assessment of risk indicators for the development of secondary ESS

Groups factors	Gradations factors	Main group		Control group		Likelihood ratio	Range risk	
		abs.	R1	abs.	R2		min	max
		51	P1=pi/n	38	P2=pi/n	P1/P2	R int	R int
Women/men	men	11	0.22	8	0.21	1.05	0.99	1.05
	women	40	0.78	30	0.79	0.99		
Age	up to 30 years	13	0.25	11	0.29	0.86	0.87	1.38
	30-40	17	0.33	9	0.24	1.38		
	over 40	21	0.41	18	0.47	0.87		
BMI	norm	21	0.41	11	0.29	1.41	0.78	1.41
	excess weight	15	0.29	13	0.34	0.85		
	obesity	15	0.29	14	0.37	0.78		
Anamnesis	DFM	19	0.37	29	0.76	0.49	0	4.6
	radiation therapy	4	0.08	2	0.05	1.6		
	operation	12	0.23	2	0.05	4.6		
	DFM+rad/t	6	0.12	4	0,1	1,2		
	DFM+oper.	4	0.08	0		0		
	oper+rad/t	2	0.04	0		0		
	other	4	0.07	1	0.03	2,3		

Number of pregnancies	up to 3	20	0.5	7	0.23	2.17	0.5	2.17
	more than 3	8	0.2	12	0.4	0.5		
	No	8	0.2	9	0.3	0.67		
	infertility	4	0,1	2	0.07	1.43		
Complaints	headache	48	0.94	37	0.9	1.04	0.46	1.04
	vision impairment	17	0.33	15	0.39	0.85		
	menstrual disorders	18	0.45	16	0.53	0.85		
	hypothyroidism clinic	11	0.22	9	0.24	0.92		
	weight gain	6	0.12	10	0.26	0.46		
Hyperprolactinemia in men	No	6	0.55	3	0.38	1.45	0.29	1.45
	There is	2	0.18	5	0.63	0.29		
Hyperprolactinemia in women	No	19	0.48	12	0.4	1,2	0.7	1,2
	There is	13	0.33	14	0.47	0.7		
Lactorea	No	30	0.75	18	0.6	1.25	0.63	1.25
	There is	10	0.25	12	0.4	0.63		
Overall score							5.72	16.53

Thus, the integrated and prognostic analysis showed that the leading risk factors in the development of secondary ESS are: a history of surgical treatment of pituitary micro- and macroadenomas (Rint=4.6), number of pregnancies up to 3 (Rint=2.17), then in descending order normal body weight (Rint=1.41), age of patients from 30 to 40 years (Rint=1.38), men (Rint=1.05), presence of headaches (Rint=1.04).

After calculating the minimum and maximum risk indicators for the formation of the ESS, we determined the calculation of the risk range for all the above factors. The formation of risk groups is carried out according to 3 risk levels: low, medium, high. For each of these groups, the risk range is calculated as follows (Table 2):

Table 2

Calculation of risk groups for the formation of secondary ESS

Risk level	Risk Range Calculation Range limits	Subranges
Short	5.72+(16.53-5.72) X 30:100=8.96	5.72-8.96
Average	5.72+(16.53-5.72) X 60:100=12.21	8.97-12.21
High	Greater than or equal to 12.22	12.22-16.53

Thus, the risk range for developing of the secondary ESS syndrome is from 5.72 to 16.53.

The division into subranges made it possible to identify patients with different risk probabilities given existing risk factors.

- low risk – from 5.72 to 8.96 – the criterion of "favorable prognosis". In patients falling within this range, the influence of risk factors is minimal.
- average risk – from 8.97 to 12.21. Patients who fall into this subrange are already more likely to develop of the secondary ESS. They should be the focus of doctors' attention.

• high risk – from 12.22 to 16.53. In this subrange, the influence of risk factors is maximum and patients who fall into it have an unfavorable prognosis for the development of the secondary ESS

Conclusion:

1. SESS syndrome is more common in men aged 30 to 40 years, with headaches, after surgery for micro- and macroadenomas of the pituitary gland.
2. Conducting an integrated assessment of risk factors will facilitate a comprehensive approach to the problem of preventing the occurrence of the secondary ESS.
3. Practical healthcare will have the opportunity to analyze the clinical characteristics of the patient and, based on the available data, determine the degree of risk of developing of the secondary ESS, predict the dynamics of its development, and carry out its prevention already at the early stages of the disease.

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