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Svitlana Shuliatytska

Ivano-Frankivsk National
Medical University, Department
of Obstetrics and Gynecology
Named after I. Lanovyi, Ivano-
Frankivsk, Ukraine

Optimization of diagnostic and treatment algorithm in adolescent girls with menstrual cycle disorders on the background of thyroid dysfunction

Svitlana Shuliatytska

Abstract

Resume: Thyroid dysfunction is accompanied by a variety of reproductive health disorders.

Purpose of the study: is to develop a programme of preventive treatment measures at different ages of puberty in adolescent girls with diffuse endemic goiter and menstrual disorders.

Materials and methods of research: 120 patients with menstrual dysfunction on the background of diffuse endemic goiter were divided into two groups. The key points of the optimized treatment complex in the main group were the use of *Agnus castus* extract. The girls in late puberty were offered low-dose combined oral contraceptives – ethinylestradiol 0.02 mg and drospirenone 3 mg in 24+4 schedule, in combination with vitamin B8 (inositol).

Results of the study and their discussion: The development of menstrual disorders (irregular periods), uterine bleeding, hypomenstrual syndrome and secondary amenorrhea, excess body weight in over half of the patients, polycystic changes in the structure of the ovaries were revealed. The scientific search allowed to note after 12 months from the beginning of therapy the decrease of a palpable struma by 1.5 times, the number of cases of galactorrhea and mastopathy decreased by 1.8 times, the normalization of hormonal imbalance, which allowed restoring menstrual function and physiological ovulatory rhythm cycles by 91.7%

Conclusions: The research results confirm that teenage girls with diffuse endemic goiter are at high risk for developing menstrual disorders but application of advanced diagnostic and preventive medical measures, enhanced by us, can improve their effectiveness and prevent reproductive disorders.

Keywords: pubertal period, diffuse endemic goiter, menstrual disorders, hormonal imbalance, treatment

Introduction

The harmonious development of a girl's body, the condition of her somatic and reproductive health status, in many respects, determine a woman's subsequent life, either in medical, sexual or social aspects [1-3, 6]. In fact, in childhood and adolescence, the preconditions for the realization of possible predictors of reproductive disorders are developed. The relationship between the ovaries and the thyroid gland at different ages and the diversity of connections they provide attract the attention of many researchers, as thyroid dysfunction is accompanied by various disorders of reproductive health: delayed sexual development, menstrual disorders, reproductive disorders and infertility in the future [1, 2, 5]. The precondition for the correction of menstrual function is the restoration of the balance of thyroid hormones, metabolic disorders, adequate uterine blood flow, along with the approximation to the reference values of the hypothalamic-pituitary link and steroidogenesis.

Given the above, the study of the structure and features of disturbances of the formation of menstrual function and the reproductive system as a whole in girls under iodine deficiency [1, 6, 7], as well as the development of a survey and monitoring tactics for such adolescents, taking into account regional peculiarities, is rather relevant and became the subject of this scientific search.

Purpose of the study

Is to develop a programme of preventive treatment measures at different ages of puberty in adolescent girls with diffuse endemic goiter and menstrual disorders and to evaluate its effectiveness in the correction of hormonal imbalance.

Materials and methods of research

As a result of our research, we have developed a screening programme that included a

Corresponding Author:

Svitlana Shuliatytska

Ivano-Frankivsk National
Medical University, Department
of Obstetrics and Gynecology
Named after I. Lanovyi, Ivano-
Frankivsk, Ukraine

screening-selection of adolescents to the risk group with the development of thyroid pathology, dispensary of girls with iodine deficiency and impaired sexual development against their background, monitoring and differentiated programme for the correction of metabolic disorders. To evaluate the effectiveness of the proposed treatment and preventive programme, 120 patients with menstrual disorders and diffuse endemic goiter were randomly divided into two groups, depending on the treatment programme: the main study group (60 girls) and the comparison group (60 girls). The control group consisted of 30 girls of similar age without concomitant somatic and gynecological morbidity. The correction of thyroid dysfunction was performed traditionally with the use of potassium iodide, and in case of absence of effect – levothyroxine with the selection of an adequate dose according to the TSH level. The key points of the optimized treatment complex in the main group were the following: the girls from the risk group at early puberty were recommended to correct menstrual function using *Agnus castus* extract to prevent the development of stressful imbalance of sex hormones (the cause of cyclical disorders) and to normalize the ratio of follicle-stimulating hormone, luteinizing hormone and prolactin. To ensure anti-stress and antioxidant effects, glycine in combination with coenzymes and L-carnitine, was administered to all girls.

The girls in late puberty were offered low-dose combined oral contraceptives – ethinylestradiol 0.02 mg and drospirenone 3 mg in 24+4 schedule; and in the case of lutein phase deficiency, progesterone was prescribed sublingually in combination with vitamin B8 (inositol) [4].

The cause for choosing this particular combination of components was the prevention of the development of polycystic ovarian transformation, premenstrual syndrome and reduction of early signs of hyperandrogenism, antidepressive and adaptive effect [4].

In the course of scientific research, the general clinical, functional and instrumental methods of examination, evaluation of features of blood circulation of the pelvic organs, ultrasound markers of the endometrial state, the study of the level of pituitary hormones and indicators of steroidogenesis, as well as the criteria of thyroid dysfunction by method of enzyme immunoassay, were used. General clinical and laboratory examination in groups was performed in combination with the assessment of hormonal status, level of mono amines (adrenaline, noradrenalin), indicators of ultrasound examination of the thyroid gland, uterus and ovaries, and oplerometry of uterine and radial arteries. For objective evaluation of the study results, the variable-based statistical method of analysis of the results using the application programme “Statistica for Windows®-6.0” was used.

Results of the study and their discussion

The presented results of the scientific search made it possible to identify and evaluate changes in the functioning of the pituitary-gonadal system in patients with thyroid dysfunction on the background of diffuse endemic goiter, which led to the development of menstrual disorders in the form of irregular menstruation cycle ($\chi^2=8.2$, $p=0.01$), uterine bleeding ($\chi^2=3.6$, $p=0.05$), hypomenstrual syndrome and secondary amenorrhea; over half of patients were diagnosed with overweight and polycystic ovarian changes.

A significant deviation from the age norm of all uterine body size and endometrial structure (its thinning) during the whole

period of formation of menstrual function in adolescent girls with endemic goiter was revealed. It proves insufficient estrogenic saturation of the body in early puberty with some data fitting to the reference value to more “mature” period, which is a strong confirmation of the influence of iodine deficiency on the processes of follicle maturation and the formation of reproductive function. There were no signs of ovulation in the dynamics of adolescent girls, whereas the girls of control group had ovulatory cycles in 36.7% of observations during the first two years of puberty, and in the stage of establishing a cyclic rhythm - in 93.3% of cases.

Steroidogenesis deficiency on the background of chronic anovulation has contributed to prolonged production of LH, testosterone, the development of early signs of hyperandrogenism, which demonstrates not only an increase in testosterone levels, but also a deficiency of sex-binding globulin in serum. The transient increase in prolactin levels in late age in girls with thyroid dysfunction, especially against the background of the chronic stress state of the psychological component, as well as significantly high rates of cortisol and glucocorticoid imbalance, should be taken into account. Reduction of estradiol and progesterone can be considered as one of the mechanisms of menstrual dysfunction in this category of patients, as well as an increase in the number of hyperproliferative processes of target organs, in particular the breast.

Thus, it should be noted that hormonal test results confirmed significant differences in the study groups: adolescents with regular menstrual cycle had normal basal levels of gonadotropins and steroid hormones in the serum, whereas patients with menstrual disorders on the background of endemic goiter demonstrated markers of discoordination of hypothalamic-pituitary-adrenal system activity, imbalance of follicle-stimulating, luteinizing hormones and prolactin synthesis, increased level of cortisol and individual monoamines, and manifestations of a hyperanogenic state. The results obtained were taken into account in the development of the algorithm of treatment and preventive measures.

The scientific search allowed to note after 12 months from the beginning of therapy the decrease of a palpable struma by 1.5 times against the initial data (66.7%); similar differences were noted in the diagnosis of palpable goiter of grade 2 due to the increase of the lobe of grade 1 goiter ($p<0.05$). The condition of skin appendages significantly improved, in particular the dryness of skin decreased by 1.4 times against data of comparison group ($p<0.05$), cephalgia cases decreased by 2.6 times ($p<0.05$), galactorrhea and mastopathy cases decreased by 1.8 times ($p<0.05$). It is important to note the tendency for weight loss in overweight girls. The regulation of menstrual cycle was observed after 12 months in 44 adolescents (73.3%) against 28 observations (46.6%) in the comparison group girls ($p < 0.05$).

Thus, the obtained results of the evaluation of the effectiveness of the proposed treatment and diagnostic algorithm and preventive programme demonstrated the normalization of indicators of hormonal status of the reproductive system, functional ability of the thyroid gland, as well as uterine hemodynamics after differentiated treatment, which allowed to restore menstrual function and physiological ovulatory rhythm of cycles before the end of puberty by 91.7% (against 68.3% in the comparison group).

Conclusion

Dissociation of the thyroid system and hypothalamic-pituitary-ovarian axis determine disorders of the menstrual cycle, the development of functional cysts and multifollicular structure of the ovarian tissue, and in the case of hypothyroidism can be considered as factors of metabolic disorders and polycystic ovary syndrome. On the other hand, functional disorders of the reproductive system and alteration of steroidogenesis can initiate the increase of thyroid dysfunction, and all the above makes it expedient to study the mechanisms of dysregulation of menstrual function in patients with diffuse endemic goiter. All the mentioned issues are rather complex and require specification and deeper evaluation.

The research results prove that teenage girls with diffuse endemic goiter are at high risk for developing menstrual disorders but application of advanced diagnostic and medical-preventive measures, enhanced by us, can improve their effectiveness and prevent reproductive disorders.

The designed clinical and diagnostic algorithm and differentiated approach to medication correction of hormonal imbalance at the difference of age stages of the puberty period allowed restoring menstrual function in 91.7% of observations against 68.3% of cases in the comparison group.

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