Why hypoestrogenism in young women is so important?

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Abstract
Hypoestrogenism is referred to lower than normal serum levels of estrogen. Hypoestrogenism can be regarded as typical and physiological in postmenopausal women. However, hypoestrogenism which occurs in young women is related to pathological background. There are two groups of disorders in young women related to hypoestrogenism: hypogonadotropic hypogonadism and hypergonadotropic hypogonadism. Hypogonadotropic hypogonadism includes hypothalamic amenorrhea, hyperprolactinemia. Hypergonadotropic hypogonadism includes gonadal dysgenesis and premature ovarian failure. Hypoestrogenism has short-term but also more long-term negative consequences for young women’s health. It concerns skeletal system, cardiovascular system and mental problems. Young women with hypoestrogenism suffer from impairment of peak bone mass achievement, decrease of bone mass density (BMD), increase risk of bone fracture. Regarding cardiovascular system these patients are characterized by endothelial dysfunction, abnormal lipid profile. Mental disorders include depressive mood, anxiety and sexual dysfunction. Proper treatment can have positive effect on reproductive function, bone status, cardiovascular and mental health in young women.

Key words: hypoestrogenism, bone, cardiovascular system, mental health, hypothalamic amenorrhea, gonadal dysgenesis

Hypoestrogenism
Hypoestrogenism is referred to serum levels of estrogens lower than normal [1]. Hypoestrogenism can be regarded as physiological in postmenopausal women [1]. However, hypoestrogenism which occurs in young women is related to pathological background. There are two groups of disorders in young women related to hypoestrogenism: hypogonadotropic hypogonadism and hypergonadotropic hypogonadism.

The below listed disorders can be regarded as clinical confirmation of hypoestrogenism. These hormonal disorders are characterized by profound hypoestrogenism with serum estradiol levels lower than 30-40 pg/ml [2].

Secondary ovarian insufficiency:
1) Hypothalamic amenorrhea:
   - functional hypothalamic amenorrhea (related to weight loss, related to stress, related to excessive exercise),
   - organic causes (tumors),
   - genetically determined (Kallmann syndrome, idiopathic hypogonadotropic hypogonadism).
2) Anorexia nervosa.
3) Hyperprolactinemia.

Primary ovarian insufficiency:
1) Gonadal dysgenesis, ovarian hypoplasia
2) Premature ovarian failure:
   - genetically determined,
   - iatrogenic causes (after chemotherapy, radiotherapy and surgical castration),
   - idiopathic.

Hypoestrogenism has short-term but also long-term negative consequences for young women’s health. It concerns skeletal system, cardiovascular system and mental problems. Young women with hypoestrogenism suffer from impairment of peak bone mass achievement, decreased bone mass density (BMD), and increased risk of bone fracture [2]. Regarding cardiovascular system, these patients are characterized by abnormal lipid profile [3]. Mental disorders include depressive mood, anxiety and sexual disturbances [4].

Hypoestrogenism and bones
Peak bone mass (PBM) represents the maximal amount of bone mineral content, gained during skeletal growth as well as the consolidation that constitutes beyond attainment of final height [5]. Achievement of optimal PBM density is of crucial significance for bone...
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Many endogenous and exogenous factors contribute to PBM formation. Endogenous factors include genetic factors, gender and hormonal factors [6]. Nutrition, physical activity and iatrogenic causes can constitute exogenous factors determining PBM formation [6]. Sex steroid (estrogen, androgen) and growth hormone (GH), insulin growth factor 1 (IGF-1) are regarded as main hormones affecting PBM formation [6]. In general, estrogen causes: activation of bone remodeling units, suppression of bone resorption and stimulation of bone formation [7].

All types of hypothalamic amenorrhea due to profound hypoestrogenism can be related to decrease in bone mass density (BMD), what is expressed in criteria of osteopenia or osteoporosis [8]. Patients with Kallmann syndrome also are threatened by BMD decrease [9].

In adult community of women with anorexia nervosa (AN) osteoporosis occurs in as many as 38% and osteopenia in 92% at one or more sites [10]. More than 50% of all women with AN have BMD below the fractures threshold and 7-fold greater fractures risk compared with matched healthy controls [11]. Lucas et al. [12] reported a 57% cumulative incidence of fractures at the spine, hip and radius 40 years after diagnosis of AN.

Patients with untreated hyperprolactinemia are also characterized by BMD decrease [13]. It is very essential to stress that young women diagnosed with hypergonadotropic hypogonadism are threatened by increased risk of osteopenia and osteoporosis.

Generally, young women with primary hypoestrogenism presents 20-30% decrease in BMD [14]. Ross et al. [15] revealed that patients with Turner’s syndrome (TS) are characterized by 3 times higher fracture risk than healthy women at the same age [15]. Hypoestrogenism is the main cause of osteopenia and osteoporosis in these patients. There is a reduction in PBM by 25% in women with Turner syndrome. Ross et al. [15] noted a significantly decreased bone density in prepubertal girls with TS compared with chronological and bone age-matched control.

Young women with premature ovarian failure (POF) should be consider as a potential group risk for osteopenia and osteoporosis. According to Nelson et al. [16] study 67% patients with POF have osteopenia.

Cardiovascular system

Cardiovascular system changes are seen mainly in postmenopausal women. However, young women with hypoestrogenism also can present some cardiovascular disturbances.

As it is known, hypoestrogenism can interfere with cardiovascular system function in many ways. Coronary and peripheral vessels contain estrogen receptors that permit estradiol to play a regulatory role in vascular function. Estrogen excites the synthesis of nitric oxide (NO) through both genomic and nongenomic effects, leading to augmented production of endothelial-derived NO, causing vasodilatation [17].

Several investigators have demonstrated a correlation between functional hypothalamic amenorrhea (FHA) and endothelial dysfunction [18]. It was clearly shown, that flow-mediated dilation of brachial artery (which is precise predictor of coronary endothelial dysfunction) is impaired among women with FHA [18]. Recently it was shown that young athletes with chronic hypoestrogenemia displayed impaired peripheral vascular function which was combined with lower resting blood pressures and heart rate and reduced ischemic responses to occlusion challenge compared to ovulatory women [3]. Turner syndrome patients also present some changes in cardiovascular system. Gravholt et al. [19] suggested that a subset of TS may have an unfavourable haemostatic balance, which may contribute to the increased risk of premature ischaemic heart disease and possibly increase the risk of deep venous and portal vein thrombosis.

Another interesting problem is that patients with profound hypoestrogenism such as Turner syndrome patients and patients with FHA present atherogenic lipid profile [20, 21]. The problem of impact of hypoestrogenism in young women on cardiovascular system requires further studies.

Mental problems

Sex steroids hormones, particularly estradiol have important direct and indirect (through neuropeptides and neurotransmitters) influence on brain function. It can have implication for clinical impact on mood changes, cognitive function, and concentration.

Gilles and Berga [22] assessed the association of cognitive function, emotional, and psychiatric history in women with functional hypothalamic amenorrhea compared with amenorrheic and eumenorrheic controls. Women with FHA endorsed more dysfunctional attitudes, had greater difficulty in coping with daily stresses, and tended to endorse greater interpersonal dependence than eumenorrheic women.

Patients with FHA and AN present common psychopathological aspects. They include maturity issues, social
insecurity and introversion, a tendency to depression, excessive concerns with dieting, and fear of gaining weight [23].

Patients with gonadal dysgenesis can also present some problems related to mood changes. Girls with TS should also be supported psychologically by social, educational and psychotherapeutic interventions, which aim to address their self-esteem and emotional difficulties [24]. Additionally patients with Turner syndrome are characterized by impairment of sexual life. Women with TS are less likely to be involved in sexual activity, arousal dysfunctions being their main symptom [25].

Conclusions

Hypoestrogenism is very important finding in young women. It always should be precisely diagnosed and managed. Proper treatment can have positive effect on reproductive function, bone status, cardiovascular and mental health in young women.

References


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