Ovarian reserve assessment in girls and women after hematopoietic stem cell transplantation (HSCT) treatment underwent in childhood

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The authors have NOTHING TO DISCLOSE.

Background

Gonadal dysfunction is the most frequent endocrine complication in long-term female survivors of hematopoietic stem cell transplantation (HSCT). It had been thought that young age prevented from ovarian damage during HSCT. The analysis performed in children after HSCT in ALL has shown that in about 80% of these children there is an impairment of gonadal function. In girls the visual pubertal development may be adequate, but menstruation is only achieved in half of the cases (12,13). It is not known if the ovarian reserve in girls and young women after HSCT leaves unaltered.

The classical tests used to evaluate the ovarian reserve have some inconvenience, especially in young patients after HSCT. Serum levels of follicle-stimulating hormone (FSH), inhibin B and estradiol are changed and should be performed in the early follicular phase. Nevertheless, the changes of serum levels of FSH, inhibin B, and estradiol occur relatively late. It is not until six months after HSCT that these hormones are abnormal (12).

Hormonal assessment of ovarian function (OF) is a relatively new marker of the ovarian function and the ovarian reserve. This is the serum marker that reflects the number of follicles that have made the transition from the primordial pool into the growing follicle pool, and that is not controlled by gonadotropins. AMH is the earliest marker of diminishing ovarian reserve, with relatively minimal intra- and inter-study variation, and its serum levels decrease well before any increase in baseline FSH. There is a transient rise in AMH in the neonatal period due to a transient activation of the reproductive axis at that time, followed by a more sustained rise through childhood and adolescence. Some studies reported that there is a plateau or even a decline in AMH during puberty. AMH continues to rise after adolescence, with peak concentration, at approximately, the age of 24, and then decrease gradually with age, and the levels become undetectable after menopause. AMH expression is affected relatively little by use of the oral or vaginal administration of synthetic sex steroids. Additionally being not controlled by gonadotropins, AMH would benefit both patients and clinicians.

Objective

The aim of the study was to assess ovarian reserve in young patients after HSCT using evaluation of AMH hormone with comparison to classical hormonal tests.

Methods

Patients

Twenty-eight girls and women, mean 14.85±3.0 y old, after HSCT, and 28 healthy girls and women, mean 15.3±3 y-old were included in the study (Table 1). The study group consisted of patients who had undergone HSCT during their early follicular phase and healthy controls, included in the control group.

Table 1. Results of ovarian function (OF) assessment in patients after autologous and allogeneic HSCT.

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</thead>
<tbody>
<tr>
<td>0-5</td>
<td>Autologous</td>
<td>8.1±3.2</td>
<td>39.8±28.0</td>
<td>5.5±3.2</td>
<td>11.1±3.5</td>
<td>1.6±0.9</td>
<td>0.8±0.5</td>
<td>0.7±0.3</td>
<td>Normal menstrual cycle</td>
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<tr>
<td>0-5</td>
<td>Allogeneic</td>
<td>10.3±3.8</td>
<td>41.8±29.2</td>
<td>4.5±2.8</td>
<td>11.5±3.6</td>
<td>1.7±0.9</td>
<td>0.8±0.5</td>
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November 28 patients (68%) had inhibin B level lower than the lowest inhibin B level in the control group. Twenty-four (86%) patients after HSCT had inhibin B level lower than 40 pg/mL, which result allows to diagnose impaired ovarian function and decreased ovarian reserve [12].

EIGHTEEN patients presented with hypergonadotropic hypogonadism, 328 patients presented with female sex hormones (including 326 prepubertal). On the basis of the results of gonadotropins, abnormal ovarian function and decrease ovarian reserve can be diagnosed in 75% of patients after HSCT.

Conclusions

Patients after HSCT have impaired ovarian reserve. The ovarian reserve is mostly related to the conditioning therapy before HSCT. AMH as well as inhibin B and FSH are specific and good markers for the assessment of ovarian reserve.

Our study results demonstrate that in young women, HSCT recipients AMH is independent and more sensitive and specific text other markers in the evaluation of ovarian function and decrease after HSCT. The measurement of AMH level allows to suspect hypogonadism in prepubertal girls, to diagnose central or compound hypogonadism, moreover lets to diagnose the ovarian reserve in the patients receiving HRT, without discontinuation of this therapy.

Acknowledgements

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Table 2. Table of ovarian function (OF) assessment in girls and women after autologous and allogeneic HSCT.

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</table>

Results

AMH and inhibin B levels were significantly lower in FSH and LH levels were significantly higher in patients after HSCT than in age-matched healthy controls. TSH, estradiol, and T4 levels were within normal limits (14).

Statistical analysis

The aim of the study was to assess ovarian reserve in young patients after HSCT using evaluation of AMH hormone with comparison to classical hormonal tests.

The decreased ovarian reserve was defined as the occurrence of elevated gonadotropins (mainly FSH), decreased inhibin B and decreased AMH levels.

Statistical analysis

Statistical analysis was performed using the Stat Soft Statistica 12.0 package. T-Student test was used for the analysis.

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