Hormone replacement therapy and intraocular pressure

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Abstract

Objectives: To evaluate the effect of hormone replacement therapy (HRT) on intraocular pressure (IOP) in menopausal women. Methods: The IOP of 25 white menopausal women without an abnormal ophthalmologic history was measured before and during HRT regimen. IOP fluctuations were recorded before and 1, 4, and 12 weeks after the beginning of HRT. These measurements were obtained according to a standardized time schedule (08:00, 12:00, 16:00, and 19:00 h). Results: The mean IOP in the left eye decreased from 16.2 ± 2.4 mmHg before therapy to 14.0 ± 2.1 mmHg after 12 weeks of therapy (P < 0.001). In the right eye, whose IOP was at 15.3 ± 2.3 mmHg before therapy there was a decrease to 14.0 ± 1.9 mmHg after 12 weeks of therapy (P < 0.001). Conclusion: Hormone replacement therapy has a positive effect on IOP in menopausal women. © 1997 Elsevier Science Ireland Ltd.

Keywords: Intraocular pressure; Menopause; Hormone replacement therapy; Nitric oxide

1. Introduction

A number of studies exist that indicate an association between intraocular pressure (IOP) and female sex hormones or a deficiency of some of these hormones [1]. A gender-based comparison of patients with IOP of more than 22 mmHg found that an increase in pressure is more frequent in women than in men [2]. As an increased IOP is usually first observed when a refraction necessitating a patient's first pair of reading glasses is determined at an age when menopausal symptoms tend to occur, this suggests a connection between a decrease in serum levels of sex steroids and changes in IOP.
Investigators have reported changes in IOP during the menstrual cycle [3,4] and the successful use of C-18 and C-21 steroids in glaucoma patients [5], suggesting a possible relationship between IOP and sex steroids. However, little information is available as to whether hormone replacement therapy (HRT) affects IOP. We performed this prospective clinical study to evaluate the influence of HRT on the IOP in menopausal women with a normal ophthalmologic history to get a basis for further clinical studies on glaucoma patients.

2. Materials and methods

In a prospective study (February 1995–February 1996), 25 whitewomen with a mean age of 55.7 ± 4 years were examined. Patients were admitted to our outpatient clinic for menopausal problems and osteoporosis prophylaxis at the Vienna University Hospital’s Department of Obstetrics and Gynecology. The study was conducted according to the guidelines of the Helsinki Declaration on Human Experimentation (1975) and all women were informed about the study and signed the written informed consent. All had reached menopause, as documented by an absence of menstrual bleeding for more than 6 months, FSH levels exceeding 30 mU/ml, and estradiol levels below 30 pg/ml. The main symptom reported was hot flushes. No patient had received any hormonal treatment for at least 1 year before the study. None of the subjects had any previous eye disease or was taking any kind of local or systemic medication with a potential influence on IOP such as β-blockers, clonidine, or carbonic anhydrase inhibitors.

Intraocular pressures were measured in the 25 subjects before as well as 1, 4, and 12 weeks after the commencement of HRT. Measurements were obtained on a standardized time schedule at 08:00, 12:00, 16:00, and 19:00 h. Intraocular pressure measurements were obtained by a single ophthalmologist with a Goldmann’s applanation tonometer (scale 1.96 mN) (Schwind Optimed, Bern, Switzerland). Applanation tonometry measures the force required to flatten a small area (diameter 3.06 mm) of the central cornea surface. The reference of physiological eye pressure values is 10–22 mmHg, with a statistical mean value of 15.5 ± 2.6 mmHg [6].

Hormone replacement therapy consisted of a constant oral dose of 2 mg estradiol valerate (Progynova®, Schering, Vienna, Austria), supplemented by ten daily doses of 10 mg medroxyprogesteronacetate (Prodafem®, Upjohn, Puurs, Belgium) during the last 10 days of each month of treatment.

To ensure compliance, we measured serum hormone levels (FSH, estradiol and prolactin) using commercial enzyme-linked immunosorbent assays supplied by Boehringer Mannheim, Vienna, Austria. Mean serum estradiol levels were 18.0 ± 9.0 pg/ml before, 34.0 ± 7.0 pg/ml after 1 week, 89.0 ± 9.0 pg/ml after 4 weeks and 91.0 ± 11.0 pg/ml after 12 weeks of therapy. The statistical group comparison was carried out using a Student’s t-test. P < 0.05 was regarded as statistically significant. For the statistical evaluation of our data we used a statistical software package provided by SAS Institute, Cary, NC. The means of the four values of each eye were used for the statistical analysis.

3. Results

As the course of HRT progressed, a decrease in IOP was observed. The results of daily pressure profiles for each eye are shown in Table 1.

In the left eye the daily mean IOP was 16.2 ± 2.4 mmHg before therapy, 15.5 ± 2.1 mmHg after 1 week, 14.7 ± 1.9 mmHg after 4 weeks and 14.0 ± 2.1 mmHg after 12 weeks of therapy. The difference of the results before therapy and after 4 and 12 weeks, respectively, were statistically significant (P < 0.001).

In the right eye, the mean IOP decreased from 15.3 ± 2.3 mmHg before therapy to 15.2 ± 2.0 mmHg after 1 week, to 14.5 ± 1.9 mmHg after 4 weeks and to 14.0 ± 1.9 mmHg after 12 weeks of therapy. The difference between results before and after 4 weeks (P = 0.007) of treatment and after 12 weeks (P < 0.001) were statistically significant.
Table 1
Mean intraocular pressure before and after 1, 4 and 12 weeks of therapy

<table>
<thead>
<tr>
<th>Time</th>
<th>Eye Pressure (mmHg)</th>
<th>LO</th>
<th>RO</th>
<th>LO</th>
<th>RO</th>
<th>LO</th>
<th>RO</th>
<th>LO</th>
<th>RO</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>08:00 h</td>
<td>12:00 h</td>
<td>16:00 h</td>
<td>19:00 h</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before HRT</td>
<td>16.2 ± 2.4</td>
<td>15.3 ± 2.3</td>
<td>16.6 ± 2.1</td>
<td>15.8 ± 2.0</td>
<td>15.9 ± 2.4</td>
<td>15.0 ± 2.7</td>
<td>15.9 ± 2.6</td>
<td>15.2 ± 2.6</td>
<td></td>
</tr>
<tr>
<td>After 1 week HRT</td>
<td>15.7 ± 2.4</td>
<td>15.4 ± 2.2</td>
<td>15.7 ± 1.8</td>
<td>15.4 ± 2.0</td>
<td>15.4 ± 1.9</td>
<td>15.2 ± 1.9</td>
<td>15.2 ± 2.4</td>
<td>14.9 ± 2.0</td>
<td></td>
</tr>
<tr>
<td>After 4 weeks HRT</td>
<td>15.0 ± 1.9</td>
<td>14.7 ± 1.9</td>
<td>15.2 ± 1.9</td>
<td>14.7 ± 1.8</td>
<td>14.4 ± 1.8</td>
<td>14.4 ± 1.8</td>
<td>14.4 ± 2.1</td>
<td>14.2 ± 2.3</td>
<td></td>
</tr>
<tr>
<td>After 12 weeks HRT</td>
<td>14.0 ± 2.1</td>
<td>14.0 ± 1.9</td>
<td>14.2 ± 1.8</td>
<td>14.2 ± 1.7</td>
<td>14.2 ± 1.8</td>
<td>14.1 ± 1.9</td>
<td>14.0 ± 2.0</td>
<td>13.8 ± 1.9</td>
<td></td>
</tr>
</tbody>
</table>

The values obtained are the means ± S.D. of each eye measured at the prescribed intervals. IOP in mm Hg; LO, left eye; RO, right eye.

The daily means of both eyes together over the entire treatment period are shown in Fig. 1.

4. Discussion

In the early 1920s, a relationship between IOP and gonadal function was first observed by Imre [7]. In subsequent studies, the relationship between IOP and the menstrual cycle, and the effects of certain hormone medications and pregnancy on IOP were examined [8]. Sano [9] observed an increase in IOP during the premenstrual phase and a decrease in IOP during ovulation. Ziai et al. [10] observed a lowering of IOP and an increase from the aqueous outflow facility during pregnancy due to a rise in progesterone. Similar results were also found in the luteal phase of the menstruation cycle [11]. This indicates that progesterone replacement may also have an IOP-lowering effect during the menopause, especially since the onset of an ovarial insufficiency in the
Menopause is initiated by a lack of progesterone.

Although these findings were the rationale for our study, the purpose was to show the impact of natural hormone preparations on IOP in menopausal women.

Intraocular pressure is maintained as the result of a balance between the secretion of aqueous humor by the ciliary processes and the reabsorption or outflow of aqueous humor through the trabecular meshwork, into Schlemm’s canal, and then through collecting channels to scleral veins [12]. The cells that line the connective tissue trabeculae of the meshwork have long been considered to play a merely passive role in the drainage process and the valve action of the outflow system. Further, it has been shown that meshwork cells have many characteristics in common with smooth muscle cells and that they contract in the presence of cholinergic agonists but relax with nitric oxide (NO) agonists [13]. Nitric oxide is an important intracellular and intercellular regulator in vascular endothelium, smooth muscle cells and certain other cell types. The endothelium in ophthalmologic vessels influences local vascular tone by releasing NO. It is worth noting that Nathanson et al., [14], have shown that the human outflow system and adjacent ciliary muscle are important sites of NO synthesis. Nitric oxide activity is associated with endothelial NO synthase located at the meshwork tissue, responsible for regulation of ocular outflow and IOP [15,16]. As a consequence of the action of estradiol, there is an increase of the endothelium-based constitutive nitric oxide synthetase. Nitric oxide and estrogen have been shown to play a critical role in the control of IOP and outflow facility and our present results suggest that NO synthase activity can be positively regulated and influenced by estradiol.

As already discussed, the incidence of increasing IOP among females rises after menopause. This rise in incidence is possibly due to a hormonal imbalance brought about by a deficiency of certain hormones like 17-β-estradiol and progesterone. Our results may be showing a new direction in the treatment of IOP.

References