NOTE

Induction of Ovulation by Sairei-to for Polycystic Ovary Syndrome Patients

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Abstract. In anovulatory patients ovulation is usually induced by clomiphene citrate (CC) or gonadotropin therapy, but in the case of polycystic ovary syndrome (PCOS), diagnosed by the presence of several micropolycysts in the ovaries and a high LH/FSH ratio in the serum, CC is only minimally effective, and side effects are often a problem with gonadotropin therapy. In the present study we administered a Chinese herbal medicine Sairei-to which appears to have a steroidal effect in anovulatory PCOS patients. As a result of the treatment, serum LH and the LH/FSH ratio significantly decreased (P<0.01) and the ovulatory rate was 70.6%. Serum testosterone levels were within normal limits before the treatment, and did not significantly change during the treatment. Sairei-to may therefore be useful for the treatment of anovulation in PCOS patients.

Key words: Sairei-to, Polycystic ovary syndrome, Ovulation, LH, LH/FSH ratio

CLINICAL findings of patients with polycystic ovary syndrome (PCOS) are well known, although its etiology remains obscure [1]. In daily clinical practice, treatment for anovulation is the main therapy for PCOS patients. Since such patients are usually non-responsive to clomiphene citrate (CC) therapy, gonadotropin therapy is apt to be employed in expectation of a great effect, but there is a risk of ovarian hyperstimulation syndrome and multifetal gestation.

In the present study we administered a Chinese herbal medicine, Sairei-to, to patients with PCOS, and examined its efficacy in ovulation induction and the resultant endocrine data.

Patients and Methods

Seventeen PCOS patients were enrolled after having given informed consent on the basis of the following three criteria: (1) irregular menstruation with anovulatory or oligoovulatory cycles in their basal body temperature (BBT) recording, (2) presence of many micropolycysts in the ovary as detected by ultrasonic examination, (3) a high level of serum LH (above 7.0 mIU/ml), FSH within normal limits (below 14.4 mIU/ml), and an LH/FSH ratio above 1.0 as assayed on the third through seventh day of the menstrual cycle. For patients who met these criteria, Sairei-to (Kanebo Ltd.) was given at a dose of 8.1 g per day for two months.

Serum LH, FSH, PRL and ACTH were examined by immunoradio-metric assay (IRMA) with radioisotope SPAC-S LH, radioisotope SPAC FSH, a SPAC-S prolactin kit (Dai-ichi Radioisotope Labo., Japan), and ACTH IRMA Mitsubishi (Yuka Medias, Japan). Testosterone, dehydroepiandrosterone
sulfate (DHEA-S), cortisol, and androstenedione (A\(^4\)A) were examined by radioimmunoassay (RIA) with a DPC total testosterone kit, a DPC DHEA-S kit (Diagnostic Products Co., USA), gammacoat\textsuperscript{TM} cortisol (Incstar Co., USA), and androstenedione RIA Mitsubishi (Yuka Medias, Japan). Statistical analysis was done by paired-T test.

Ovulation was confirmed by both BBT and transvaginal ultrasonic examination.

As control cases eight women with regular menstruation cycles were selected.

**Results**

Twelve (70.6%) of 17 PCOS patients became ovulatory. In the ovulatory cases serum LH was 12.20 ± 5.75 mIU/ml (mean ± SD) before administration and 4.15 ± 2.19 during administration. The LH/FSH ratio was 1.96 ± 0.96 before administration and 0.72 ± 0.40 during administration (Fig. 1). These decreases were statistically significant (P<0.01). Other hormonal data (FSH, PRL, ACTH, cortisol, A\(^4\)A, testosterone and DHEA-S) were within normal limits before administration, with no significant changes during administration. In the anovulatory cases serum LH decreased during administration, but not significantly. In control cases all hormonal data were within normal limits before administration, with no significant changes during administration (Table 1).

There was no change in ovarian volume or the polycystic pattern on ultrasonic examination during administration in both ovulation and anovulation groups.

Body mass index was 22.1 ± 3.86 in ovulation group, 23.2 ± 5.23 in anovulation group and 21.6 ± 4.37 in control group.

There were no side effects in any case. Three patients became pregnant after the treatment.

**Discussion**

The Chinese herbal medicine Sairei-to, which contains twelve active ingredients (Saiko, Kanzou and Keihi etc.), is reported to possess antiallergic effects, and can be used for minimizing the dose of corticosteroids in patients with nephrotic
EFFECT OF SAIREI-TO FOR PCOS

In clinical cases in obstetrics and gynecology, Sairei-to is often prescribed for patients with toxemia of pregnancy or emesis gravidarum in Japan. In a recent report Sairei-to was considered to be an effective therapy for patients with recurrent abortion who are found to be positive for antiphospholipid antibodies [5, 6]. Singh reported that the use of dexamethasone with CC induced ovulation in 88.8% of clomiphene-resistant women with PCOS [7]. Prednisone and CC treatment was also reported for patients with chronic anovulation including PCOS cases resistant to CC alone. 79% of patients became ovulatory in the study [8]. Steroidal medicine therefore seems to be effective for patients with PCOS, especially for anovulation. In expectation of the steroidal effect as proved by animal experiments [9], we administrated Sairei-to to PCOS patients. Both Serum LH and LH/FSH decreased significantly, and the ovulatory rate was 70.6%. In another 3 cases of anovulatory PCOS resistant to CC alone, the patients became ovulatory during treatment with CC and Sairei-to. Therefore it may be possible to use Sairei-to in anovulatory PCOS patients resistant to CC alone in the same way as prednison.

Another traditional herbal medicine, Shakuyaku-Kanzo-To, has been found to lower high serum testosterone levels in oligomenorrheic and anovulatory women [10-13]. In our study the serum testosterone level was not high in the pre-treated patients with PCOS. It remained uncertain whether Sairei-to may be effective in PCOS patients with high testosterone levels.

The reason why LH and the LH/FSH ratio decreased seems to be a result of improvement of irregular menstruation and anovulation. A study is necessary to elucidate its mechanism.

In summary, Sairei-to may be useful for the treatment of anovulation in PCOS patients. Further study is required to evaluate the effect of Sairei-to on hypothalamic-pituitary-ovary axis.

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Table 1. Serum gonadotropin and androgen levels before and during administration of Sairei-to in PCOS patients and ovulatory women (control)

<table>
<thead>
<tr>
<th></th>
<th>LH (mIU/ml)</th>
<th>FSH (mIU/ml)</th>
<th>testosterone (ng/ml)</th>
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</thead>
<tbody>
<tr>
<td>PCOS (n=17)</td>
<td></td>
<td></td>
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<tr>
<td>before ad.</td>
<td>12.14 ± 5.93</td>
<td>6.76 ± 2.18</td>
<td>0.43 ± 0.15</td>
</tr>
<tr>
<td>during ad.</td>
<td>5.40 ± 3.55*</td>
<td>6.16 ± 1.48</td>
<td>0.33 ± 0.18</td>
</tr>
<tr>
<td>control (n=8)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>before ad.</td>
<td>2.46 ± 1.65</td>
<td>8.22 ± 1.31</td>
<td>0.18 ± 0.08</td>
</tr>
<tr>
<td>during ad.</td>
<td>2.34 ± 1.27</td>
<td>7.72 ± 0.89</td>
<td>0.20 ± 0.10</td>
</tr>
</tbody>
</table>

The data are the mean ± SD. *: P<0.01 vs. before administration. ad.=administration.

References


