Infertility is the diminished ability or the inability to conceive and have offspring. It can also be defined as the failure to conceive after a year of regular intercourse without contraception. Infertility can be of two types: primary and secondary. Primary infertility is a term used to describe a couple who have never been able to conceive, whereas secondary infertility is a term used to describe a couple who have been pregnant at least once, but have not been able to become pregnant again.

Infertility may be caused by different factors. According to several studies, more than half the cases of infertility are the result of problems with the female partner, whereas the remaining cases are caused by sperm disorders and by unexplained factors. A woman is in the fertile phase of the menstrual cycle before and during the ovulation period and in the infertile phase during the remaining period of the menstrual cycle. Fertility awareness practices are used to discern the fertile and infertile phases of menstrual cycle by tracking changes in cervical mucus or basal body temperature.

Sterility is the inability to reproduce because of congenital or acquired reproductive system disorders involving lack of gamete formation or production of abnormal gametes. A couple that has tried unsuccessfully to have a child for a year or more is said to be subfertile. The couple’s fecundability rate is approximately 3% to 5%. Many of its causes are the same as those of infertility. Such causes could be endometriosis, or polycystic ovarian syndrome. Reproductive endocrinologists consider a couple to be infertile if the couple is not able to conceive after 12 months of contraceptive-free intercourse (when female is under the age of 34); if the couple is not able to conceive after six months of contraceptive-free intercourse (when female is over the age of 35); or if the female is incapable of carrying a pregnancy to term.

Ovulatory disorders, characterized by anovulation or by infrequent and/or irregular ovulation, are one of the most common reasons for the inability to conceive. It accounts for about 30% of infertility cases in women. Ovulation is a complex event in which hormonal signals and physical events are important. The causes of failed ovulation are mainly due to hormonal problem which is the leading cause of anovulation. For the process of ovulation to be successful, a complex balance

Key words: Evecare, infertility, estrogen
of hormones and their interactions is necessary; any disruption in these interactions can hinder ovulation. Oligomenorrhea or complete amenorrhea usually indicates ovulatory disorders. Infertility is not only a physical ailment, but also a psychological and social problem. Stress can change the hormonal levels in women and delay ovulation. Immunological factors also play a role in infertility.

Herbal therapies have been used since ancient times to treat infertility. This study was planned to evaluate the efficacy of Evecare, a herbal formulation, claimed to be effective in infertility. Evecare contains extracts of herbs such as *Saraca indica*, *Symlocos racemosa*, *Adhatoda vasica*, *Aloe vera*, *Asparagus racemosus*, *Boerhaavia diffusa*, *Bombax malabaricum*, *Cocos nucifera*, and *Tinospora cordifolia*, as its main constituents.

**Aim of the Study**

The aim of the study was to evaluate the clinical efficacy and safety of Evecare syrup in the management of female infertility.

**Material and Methods**

**Study Design**

An open clinical trial was conducted at M.L.N. Medical College Hospital, Allahabad, India in accordance with the Declaration of Helsinki and the GCP Ethical Guidelines. The study protocol, case report forms, regulatory clearance documents, product-related information, and informed consent forms were approved by the Institutional Ethics Committee.

**Inclusion Criteria**

Infertile women in the age group of 30 to 45 years who failed to conceive after a minimum of three years of regular intercourse without contraception were included in the study. Demographic data of patients on entry into the study are given in Table 1.

**Table 1. Demographic Data of Patients on Entry**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Evecare syrup (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years (mean ± SD)</td>
<td>37.60 ± 8.10</td>
</tr>
<tr>
<td>Mean weight in kg (mean ± SD)</td>
<td>48.90 ± 18.20</td>
</tr>
<tr>
<td>Duration of infertility in years (mean ± SD)</td>
<td>4.20 ± 1.40</td>
</tr>
</tbody>
</table>

**Exclusion Criteria**

Patients having anatomical defects of uterus and or cervix, uterine malignant tumors, evidence of malignancy, history of uterine surgery, pituitary tumors, and renal failure; patients with problem in the male partner; and patients who were unwilling to sign the informed consent form were excluded from the study.

**Study Procedure**

Hundred infertile patients attending the outpatient department of M.L.N. Medical College Hospital, Allahabad, India were included in the study. Routine physical and gynecological examinations, laboratory tests, and hormonal assays of follicle stimulating hormone (FSH), luteinizing hormone (LH), progesterone, and estrogen (estradiol) were carried out before and after the treatment. Patients were administered Evecare syrup at a dosage of 10 to 15 ml twice-daily for a period of six months. No other medications were given to these patients.

**Primary and Secondary Endpoints**

Conception at the end of the treatment was predefined as the primary endpoint, whereas any adverse effects (either reported or observed) during the study period was predefined as the secondary endpoint.

**Adverse Events**

All adverse events, either reported or observed by patients, were recorded with information about severity, date of onset, duration, and action taken regarding the study drug. Relation of adverse events to study medication was predefined as ‘Unrelated’ (a reaction that does not follow a reasonable temporal sequence from the administration of the drug), ‘Possible’ (follows a known response pattern to the suspected drug, but could have been produced by the patient's clinical state or other modes of therapy administered to the patient), ‘Probable’ (follows a known response pattern to the suspected drug that could not be reasonably explained by the known characteristics of the patient’s clinical state), and ‘Certain’ (the adverse events must have definitive relationship to the study drug, which cannot be explained by concurrent disease or any other agent).
Patients were allowed to voluntarily withdraw from the study if they experienced serious discomfort during the study or sustained serious clinical events requiring specific treatment. Efforts were made to ascertain the reason for dropout. Noncompliance (defined as failure to take less than 80% of the medication) was not regarded as treatment failure, and reasons for noncompliance were noted.

**Statistical Analysis**

Results were expressed as mean ± SD or as incidences of observations. Data were analyzed using Student's paired 't' test and Fisher’s exact test was used to find the level of significance. Minimum level of significance was fixed at p < 0.05. Analysis was performed using GraphPad Prism Software for Windows (Version 4.03).

**Results**

Results of the study showed a significant increase in the levels of estrogen (p < 0.0292) (Fig. 1) and progesterone (p < 0.0059) (Fig. 2) hormones and no change in the levels of FSH and LH after six months of treatment with Evecare syrup (Table 2). Seventeen of the 100 enrolled patients conceived at the end of the treatment (significance, p < 0.0001) (Fig. 3 and Table 3). No clinically significant adverse effects were observed or reported. All the patients completed the treatment regimen and there were no dropouts from the study.

**Table 2.** Changes in FSH, LH, Estrogen, and Progesterone Levels before and after Treatment with Evecare Syrup (Mean ± SD)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Before treatment</th>
<th>After treatment</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>FSH (mIU/ml)</td>
<td>11.27 ± 4.912</td>
<td>11.77 ± 5.205</td>
<td>NS</td>
</tr>
<tr>
<td>LH (mIU/ml)</td>
<td>15.41 ± 14.38</td>
<td>15.80 ± 9.42</td>
<td>NS</td>
</tr>
<tr>
<td>Estrogen (pg/ml)</td>
<td>54.31 ± 36.64</td>
<td>70.40 ± 50.56</td>
<td>p &lt; 0.0292</td>
</tr>
<tr>
<td>Progesterone (ng/ml)</td>
<td>10.65 ± 9.168</td>
<td>15.01 ± 10.78</td>
<td>p &lt; 0.0059</td>
</tr>
</tbody>
</table>

Statistical analysis was carried out using paired 't' test. Total no. of patients = 100.

**Table 3.** Pregnancy Rate before and after Treatment with Evecare Syrup

<table>
<thead>
<tr>
<th>Pregnancy rate</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-pregnant</td>
<td>100</td>
<td>83</td>
</tr>
<tr>
<td>Pregnant</td>
<td>0</td>
<td>17</td>
</tr>
</tbody>
</table>

(p < 0.0001)

Statistical analysis was carried out using Fisher’s exact test.

*p < 0.0292, as compared to pretreatment value.

*p < 0.0059, as compared to pretreatment value.

*p < 0.0001, as compared to pretreatment value.
**Discussion**

Infertility can be a traumatic experience, especially for women. As motherhood is primarily a female instinct, the inability to bear a child affects the woman's identity itself. It is estimated that about 25% of women experience infertility during their reproductive years and the number is growing every year. Female infertility may be caused by a host of factors such as ovulation problems, tubal blockage, age, uterine problems, previous tubal ligation, and unexplained reasons. Many of these factors can be effectively treated.

Ovulation depends upon a complex balance of hormones and their interactions, and any disruption in these interactions may hinder the process of ovulation. Infection caused by bacteria and viruses commonly cause inflammation of the fallopian tubes, which may contribute to infertility. For women with endometriosis, a condition characterized by excessive growth of endometrium, the monthly fecundity (chance of getting pregnant) diminishes by 12% to 36%. High amount of androgen secretion, which is more of a male hormone than female hormone, may also result in infertility. This may also cause menstrual disorders. Absence of periods or infrequent periods is the symptom of polycystic ovary syndrome. Three percent of couples face infertility due to poor quality of cervical mucus. Cervical mucus needs to be of a certain consistency and available in adequate amounts for sperms to swim easily within it. The most common reason for abnormal cervical mucus is hormonal imbalance, namely too little estrogen or too much progesterone. Certain personal preferences, habits, and lifestyle choices may impact health and may also limit a couple’s ability to conceive. For optimal functioning of the reproductive system, proper diet and exercise are necessary. Women who are significantly overweight or underweight may have difficulty in becoming pregnant. The ability to conceive may be affected by exposure to various toxins or chemicals at workplace or surrounding environment.

Abdominal diseases such as appendicitis and colitis may cause inflammation of the abdominal cavity, which may affect fallopian tubes. Pelvic or abdominal surgery can result in adhesions that alter the tubes in such a way that eggs cannot travel through them. Ectopic pregnancy occurs in the tube itself and, even if carefully and successfully overcome, may cause tubal damage.

Approximately 10% of the infertile women suffer from unexplained factors of infertility, wherein the commonly performed tests to diagnose infertility are normal and no particular reason for infertility is evident. Sometimes, even after fertilization is achieved, presence of low progesterone levels may result in underdeveloped endometrium, which may prevent implantation of the embryo.

In this study, Evacare syrup was evaluated for its safety and efficacy in the treatment of female infertility. Evacare, a herbal formulation, contains *Saraca indica*, *Symplocos racemosa*, *Adhatoda vasica*, *Aloe vera*, *Asparagus racemosus*, *Boerhaavia diffusa*, *Bombax malabaricum*, *Cocos nucifera*, and *Tinospora cordifolia* as its major constituents.

*Saraca indica* is well-known for its effectiveness in treating menorrhagia. The herb also has a stimulatory effect on the ovarian tissue, which may produce an estrogen-like activity that enhances ovulation and repair of the endometrium. *Symplocos racemosa*, which has been used since ancient times to treat menstrual and uterine disorders, exhibits relaxant and antispasmodic effects on several spasmogens of the uterine smooth muscles. It attributes favorable actions to the drug in treating dysmenorrhea and menorrhagia and also acts as a uterine sedative. *Cyperus rotundus* has been found to be effective in the treatment of anemia and in general weakness. *Tinospora cordifolia* is well known for its immunomodulatory effect and thus, helps in boosting the immune system, which indirectly increases the feeling of well-being in patients. *Aloe vera* regulates female hormones and improves fertility. The ethanolic extract of *Boerhaavia diffusa* is found to stop intrauterine contraceptive device-induced bleeding in monkeys. It is also known for its anti-inflammatory and analgesic properties, which is comparable to that of ibuprofen. The herb also acts as a hematinic. *Adhatoda vasica* is known for its antihemorrhagic activities, and thus is beneficial in dysfunctional uterine bleeding and a useful remedy in disorders of the uterus.

The combined action of all these herbs helps in ovulation, conception, and proper implantation, which
may lead to normal pregnancy. The possible mechanism of the ingredients of Evecare could be attributed to their synergistic action. The properties of the herbs also help to correct menstrual disorders, infections, dysfunctional uterine bleeding, and ovulatory defects and improve general health by correcting anemia and enhancing immunity thus correcting the infertility. The results obtained are comparable to those of clomiphene citrate.8

Conclusion

The ability to conceive and sustain pregnancy is desired by most couples in their lifetime. Most of the fertility drugs prescribed to infertile women are made from hormones and functions by stimulating the reproductive system. These drugs are mostly associated with side effects. The present open study was conducted to evaluate the safety and efficacy of Evecare syrup, a polyherbal uterine tonic, in the treatment of infertility. Results of this study indicated that Evecare promotes conception and helps to correct hormonal imbalance in infertile women without causing any adverse effects. Thus, Evecare syrup was found to be safe and effective in the treatment of infertility in women.

References