SHORT COMMUNICATION:

POSSIBLE CAUSE OF INFERTILITY—A PHARMACOLOGICAL APPROACH

S.K. Batta*, B. Mukerjee and G. Santhakumari

Departments of Pharmacology and Obstetrics and Gynaecology, Medical College, Kottayam-686008

Summary: The uterine fluid of idiopathic infertile women was subjected to pharmacological investigation. The uterine fluid obtained from 17 out of 21 infertile women had a vasodepressor activity akin to that from normal women (2) but it was either increased or decreased. Though the difference in activity in uterine fluid from normal and infertile women was not statistically significant, yet the range of activity was quite different in the two groups.

Keywords: idiopathic infertility uterine fluid vasodepressor activity

INTRODUCTION

The cause of infertility has been attributed to many factors (3). Idiopathic infertility is a term reserved for those couples in which no cause can be found in spite of dependable, complete infertility survey. The incidence of this type of infertility is 15% (3).

So far, according to literature published, there has not been any report on the pharmacological, biochemical and microbiological studies of the uterine fluid of the idiopathic infertile patients.

The present study was undertaken to investigate the pharmacological activity of the uterine fluid of the idiopathic infertile patients.

MATERIALS AND METHODS

Couples reporting for investigation in the Infertility Clinic of the Department of Obstetrics and Gynaecology, Medical College Hospital, Kottayam, were selected for study. The infertile couples were examined for any organic pathology. The individual couples were examined, interviewed and investigated to rule out endocrinological causes of infertility. The couples had a married life history of 2—14 years, and had no history of conception and contraception. The age of the female partner and the other relevant date about the cycle are presented in Table 1.

Selection of subjects: The subjects for study were selected after a thorough check-up by the gynaecologist. Male partners of the infertile couples had normal spermograms. The

*Instituto di Farmacologia-32, Via Vancielli, 20129 Milano—Italy.
TABLE I: Various parameters of idiopathic infertile women.

<table>
<thead>
<tr>
<th>Age group</th>
<th>No. of subjects</th>
<th>Period of marriage</th>
<th>No. of subjects</th>
<th>Length of menstrual cycle</th>
<th>No. of subjects</th>
<th>Length of period</th>
<th>No. of subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between 15 yrs.</td>
<td>13</td>
<td>Below 5 yrs.</td>
<td>13</td>
<td>28 to 30 days</td>
<td>19</td>
<td>Less than 4 days</td>
<td></td>
</tr>
<tr>
<td>20 and 25 yrs.</td>
<td>26</td>
<td>6 to 10 yrs.</td>
<td>6</td>
<td>More than 30 days</td>
<td>3</td>
<td>4 to 6 days</td>
<td></td>
</tr>
<tr>
<td>26 and 30 yrs.</td>
<td>6</td>
<td></td>
<td>6</td>
<td></td>
<td>3</td>
<td>4 to 6 days</td>
<td></td>
</tr>
<tr>
<td>More than 31 yrs.</td>
<td>1</td>
<td>More than 10 yrs.</td>
<td>3</td>
<td></td>
<td></td>
<td>More than 6 days</td>
<td></td>
</tr>
</tbody>
</table>

uterine fluid was taken as and when the patients came in any phase of the cycle, except menstruation. Majority of patients were in midcycle.

Collection of uterine flushing: The method of collection of uterine flushing has been described by Batta et al. (2).

The uterine lavage was tested for its pharmacological activity of the following: rat blood pressure for acetylcholine (ACh) and adrenaline-like activity isolated rat uterus for oxytocin-like activity and isolated guinea pig ileum for histamine and acetylcholine-like activity. The methods for setting up isolated tissues and the intact rat preparations and the bioassay have been described by Batta and Chaudhury (1). The volume of injection of the uterine flushings into the intact rat and the isolated tissue bath was 0.1 ml. The capacity of the tissue bath was 5 ml.

RESULTS

Rat B.P.: The Uterine flushings produced depressor response in the rat which was blocked partially (50-75%) by atropine (50 μg), while the depressor response to the ACh was blocked completely. The depressor activity of the uterine flushings was therefore, largely due to acetylcholine-like substance and is designated as ACh-LA. Ten of the 21 patients exhibited 1.0 to 3.0 μg/ml of ACh-LA and 7 exhibited 15–100 μg/ml of ACh-LA in their flushings.

One flushing sample from infertile group of women had vasopressor activity (2 μg/ml comparable to adrenaline responses, and is tentatively designated as adrenaline-like activity A-LA. Three samples of uterine flushings from infertile women exhibited biphasic activity (vasodepressor followed by vasopressor); only the vasodepressor component could be blocked partially by atropine, the data are summarised in Table II.

Isolated preparations: The uterine flushings had no effect on the isolated tissues but the subsequent sensitivity of the tissue was altered. The rat uterus became sensitized to oxytocin (0.5 mU/5ml) after the uterine flushings from infertile patients were added to the bath and the
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infertile women.

<table>
<thead>
<tr>
<th>No. of</th>
<th>Length of period</th>
<th>No. of subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>19</td>
<td>Less than 4 days</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>4 to 6 days</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>More than 6 days</td>
<td>2</td>
</tr>
</tbody>
</table>

phase of the cycle, except in

Unusual activity of the following: rat blood

ated rat uterus for oxytocin-like dopamine-like activity. The methods

d of the bioassay have been

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of the tissue bath was 5 ml.

response in the rat which was

pressor response to the ACh was

ings was therefore, largely due

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Ch-LA in their flushings.

vasopressor activity (2 µg/ml) may have been adrenaline-like activity, which exhibited biphasic activity

or component could be blocked

on the isolated tissues but the

us became sensitized to oxytocin

ed to the bath and the

A. Rat blood pressure

Vasopressor (1) 2 µg/ml A-LA

Vasodepressor (10) 1.0-3.0 µg/ml ACh-LA

B

Biphasic (7) 15.0-100.0 µg/ml ACh-LA

Normal women

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Response</th>
<th>Activity in fluid from infertile women</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Rat blood pressure</td>
<td>Vasopressor (1)</td>
<td>2 µg/ml A-LA</td>
</tr>
<tr>
<td></td>
<td>Vasodepressor (10)</td>
<td>1.0-3.0 µg/ml ACh-LA</td>
</tr>
<tr>
<td></td>
<td>B (7)</td>
<td>15.0-100.0 µg/ml ACh-LA</td>
</tr>
<tr>
<td></td>
<td>Biphasic (3)</td>
<td>1.4-2.0 µg/ml ACh-LA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.0-2.2 µg/ml A-LA</td>
</tr>
<tr>
<td>B. Rat uterus</td>
<td>Sensitization (4)</td>
<td>10-25%*</td>
</tr>
<tr>
<td></td>
<td>Sensitization (4)</td>
<td>10-25%*</td>
</tr>
<tr>
<td></td>
<td>Desensitization (5)</td>
<td>40-45%**</td>
</tr>
</tbody>
</table>

A-LA Adrenaline like activity

ACh-LA Acetylcholine like activity

* Data from Batta et al. (1972)

** Percent of sensitization or desensitization

Figures in parentheses indicate the number of subjects or preparations.

tissue washed out. The increase in sensitivity ranged from 10 to 25% (4 observations). The
guinea pig ileum was desensitized by 40 to 45% (5 observations) to histamine (0.5 µg/5 ml) and
to ACh (0.1 µg/ml).

DISCUSSION

The present preliminary study shows that the uterine flushings obtained from idiopathic
infertile patients have an altered pharmacological activity as compared to that of the uterine
fluid of normal women (2). The flushings showed vasodepressor activity like that from the
normal women (2) but the activity was either too low or very high. For purposes of compar-
ison data from the previous paper (2) are included in Table II. The low activity in the
uterine fluid was significantly less as compared to that in the normal fluid (P<0.05) while there
was no difference, when high activity group was compared to the normal (P>0.05). When
activity in flushings from the group as a whole, of infertile women was compared with that in
normals, there was no difference.

It appears from the results obtained that the vasodepressor substance present in the
uterine fluid of idiopathic infertile patients is altered, so that the proper tone of the uterus may
not be maintained leading to a failure of implantation in these patients.
The results obtained on the isolated tissues are at variance with those obtained from the uterine fluid of normal women by Batta et al. (2). The sensitisation of the rat uterus by the infertile fluid was less than that with the normal one; similarly the uterine fluid from the infertile women had a qualitatively different effect (desensitisation) on the isolated guinea pig ileum as compared to that from the normal one (sensitisation).

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REFERENCES