

SHORT COMMUNICATION :

POSSIBLE CAUSE OF INFERTILITY—A PHARMACOLOGICAL APPROACH

S.K. BATT<sup>a</sup>\*, 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.

**Key words:** 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 spermatograms. The

---

\*Istituto di Farmacologia-32, Via Vancitelli, 20129 Milano—Italy.

TABLE I: Various parameters of idiopathic infertile women.

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

uterine fluid was taken as and when the patients came in any phase of the cycle, except in 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 of the bioassay have been described by Batta and Chaudhury (1). The volume of injection of the uterine flushings in 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  $\mu$ g), 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  $\mu$ g/ml of ACh-LA and 7 exhibited 15-100  $\mu$ g/ml of ACh-LA in their flushings.

One flushing sample from infertile group of women had vasopressor activity (2  $\mu$ g/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

TABLE II: A. Response of rat blood pressure to uterine flushings.  
B. Sensitization or desensitization of rat uterus to oxytocin and guinea pig ileum to ACh or histamine by uterine flushings obtained from idiopathic infertile women.

Preparation	Response	Activity in fluid from infertile women	Normal women
A. Rat blood pressure	Vasopressor (1)	2 $\mu\text{g/ml}$ A-LA	Nil
	Vasodepressor (10)	1.0-3. $\mu\text{g/ml}$ ACh-LA	6.0-15.0 $\mu\text{g/ml}$ ACh-LA (13)
	B (7)	15.0-100.0 $\mu\text{g/ml}$ ACh-LA	Nil
	Biphasic (3)	1.4-2.0 $\mu\text{g/ml}$ ACh-LA 1.0-2.2 $\mu\text{g/ml}$ A-LA	Nil
B. Rat uterus Guinea pig ileum	Sensitization (4)	10-25%*	45.5% (6)
	Sensitization —	None	75.0-130.0% (4)
	Desensitization (5)	40-45%**	None

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  $\mu\text{g}/5\text{ ml}$ ) and to ACh (0.1  $\mu\text{g}/\text{ml}$ ).

## 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 comparison 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).

### ACKNOWLEDGEMENTS

The authors are grateful to Dr. C.M. Francis, Principal and Prof. G.Y.N. Iyer, Head of Department of Biochemistry, Medical College, Kottayam, for careful and critical review of the manuscript.

### REFERENCES

1. Batta, S.K. and R.R. Chaudhury. Observation on the intraluminal fluid obtained from rat uteri with intrauterine device in one horn. *Ind. J. Med. Res.*, **57** : 1711 1969.
2. Batta, S.K., B. Mukerjee and G. Santhakumari. Pharmacological studies on the utrine flushing in women with and without intrauterine devices. *Arch. Int. Pharmacodyn. Ther. Suppl.*, **196** : 174, 1972.
3. Wall, R.E. Evaluation and management of infertility, *Clin. Obstet. and Gynec.*, **12** : 851, 1969.