INTRAUTERINE INSEMINATION OF HUSBAND'S SEMEN

B. N. BARWIN*

*Departments of Physiology and Midwifery & Gynaecology,
The Queen's University of Belfast, Northern Ireland*

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Summary. Fifty patients with primary infertility were treated by intra-uterine insemination of the husband's semen which had been stored. Thirty patients had sperm counts of greater than $20 \times 10^6/\text{ml}$ with 50% motility and twenty patients had oligospermia ($<20 \times 10^6/\text{ml}$).

The technique of storage of semen is reported and the intrauterine method described. The rôle of the buffer solution is discussed in overcoming the complications of intrauterine insemination. A success rate of 70% is reported in the normospermic group and 55% in the oligospermic group over nine cycles of intrauterine insemination of husband's semen.

INTRODUCTION

One of the main problems confronting the gynaecologist in the investigation of infertility is the consistent finding of immotile spermatozoa, spermatozoa of low motility and low sperm count in the cervical mucus or semen (Scott, 1968). There was considerable controversy among earlier workers in the field that the sperm count was substandard if it fell below $60 \times 10^6/\text{ml}$ but MacLeod (1962) has carried out considerable research in this field and it is now generally accepted that true oligospermia is represented by counts of less than $20 \times 10^6/\text{ml}$ provided the motility is good.

SUBJECTS AND METHODS

Selection of cases

Fifty couples with primary infertility of between 3 and 14 years' duration were selected. The age distribution was between 24 and 41 years. In all cases, the wives had been subjected to a full clinical investigation. Ovulation was proven on the basis of biphasic basal body temperature records, vaginal cytology, cervical mucus studies, endometrial biopsies and, where indicated, steroid urinary assays. Tubal patency was confirmed by hysterosalpingogram and laparoscopy hydrotubation.

In twenty couples, a male factor was present on the criterion of two negative

* Present address: Department of Obstetrics & Gynaecology, University of Ottawa, Ottawa General Hospital, 43 Bruyere Street, Ottawa, Ontario, Canada K1N 5G7.

postcoital tests and two oligospermic semen specimens according to the criteria of Eliasson (1971). These patients were allocated to two groups—low grade oligospermia (counts $<10 \times 10^6$ spermatozoa/ml with 50% motility) and high grade oligospermia (counts between 10 and 20×10^6 spermatozoa/ml with at least 50% motility).

In eighteen of the remaining thirty couples where a normal sperm count was recorded, a cervical mucus factor was thought to be responsible for the infertility (Parrish & Ward, 1968). This was based on the finding of negative post-coital tests on at least two occasions where immotile spermatozoa were found in the cervical mucus at mid-cycle. The cervical mucus invasion test was also negative on two occasions. Semen analysis in this group was normal on two occasions (sperm count $>20 \times 10^6$ /ml with 50% motility).

The indications for intrauterine insemination of husband's semen (AIH) are given in Table 1.

Technique of storage

In all cases, following a period of 3 days' abstinence, at least two samples of semen were produced by masturbation and collected into a plastic leak-proof container. The samples were examined for sperm motility and concentration within 1 hr of ejaculation. Only specimens with at least 50% motility were selected for storage. Specimens were stored separately in a freshly prepared buffer solution made up as follows. For 1000 ml of buffer, the following concentrations were required: germ-free egg yolk, 200 ml; glycerol, 140 ml; glucose (5%), 264 ml; sodium citrate (2.9%), 396 ml; streptomycin, 500 g; glycol, 20 g.

The above solution was gently heated for 30 min to dissolve the constituents and was then allowed to cool to 35° C. Sodium bicarbonate was added until a pH of 7.2 to 7.4 was achieved. The buffer was then added in equal volumes with the semen. This procedure was carried out under sterile conditions. The diluted semen was cooled to 18° C before freezing. Plastic tubes known as 'straws' were filled with semen—each straw being 10 cm long and having a volume of $\frac{1}{2}$ ml. The patient's name was stamped on the straws and each straw was heat-sealed. The straws were then placed in a metal rack and frozen in the vapour of a large liquid nitrogen vessel to -150° C. On average, fifteen straws were required for each diluted specimen. This method of freezing was developed by the Artificial Insemination Centre at L'Aigle in France (Cassou, 1959) and is the method used by the Artificial Insemination Centre in Northern Ireland. A similar method has been described by Behrman & Sawada (1966).

When required for AIH, the specimens of semen were removed from the liquid nitrogen and thawed out to 35° C. One straw from each batch was examined. There was a 5 to 10% loss of motility after thawing the semen.

Timing of insemination

Before the commencement of AIH, the average mid-cycle day was calculated from observation over a period of 3 consecutive months. The patients were instructed to contact the author 2 days before the presumed mid-cycle day (i.e. 2 days before the rise of basal body temperature). In ten cases, 20 mg

conjugated oestrogen ('Premarin') were administered by intravenous injection over 3 min on Days 10 to 12 of the cycle as described by Foldes (1972). Cervical mucus was also studied for spinnbarkeit and ferning.

Insemination was performed daily 2 to 3 days ahead of ovulation until the basal body temperature had risen to its post-ovulation level. A sterile mixing needle was introduced into the uterine cavity and 0.1 to 0.3 ml thawed semen and buffer was inserted into the uterine cavity. The remaining semen and buffer, 1 to 1.5 ml, were inserted into the cervical canal and vagina. The patient remained in the lithotomy position for 20 to 30 min. Where a cervical mucus factor existed, the cervical mucus was aspirated and 0.1 to 0.3 ml of husband's semen and buffer was introduced into the uterine cavity.

RESULTS

The results are summarized in Tables 1 and 2. The overall success rate was 62%. Table 1 shows the results of insemination where analysis indicated a

Table 1. Results of AIH when semen analysis showed a 'normal'* sperm count

<i>Specialist referral</i>	<i>Indication</i>	<i>No.</i>	<i>No. of inseminations/cycle</i>	<i>Result</i>	<i>% success</i>
Urologist	Retrograde ejaculation	1	4.0	0	0
Neurologist	Impotence (paraplegics)	5	3.0	3 pregnant†	60%
Radiotherapist	Seminoma	3	3.5	2 pregnant	66%
Psychiatrist	Vaginismus (1) Impotence (2)	3	2.5	2 pregnant	66%
Infertility clinic	Cervical mucus factor	18	3.5	13 pregnant‡	70%
Total		30	3.3	20 pregnant	66%

* $> 20 \times 10^6$ spermatozoa/ml and 50% motility.

† There was one abortion.

‡ There were two abortions.

'normal' sperm count ($> 20 \times 10^6$ spermatozoa/ml with 50% motility). In this group, five patients with impotence due to neurological factors were selected. The husbands were able to masturbate and the semen was stored as described in the 'Methods' section. In this group, three pregnancies resulted although one aborted at 12 weeks' gestation. In the case of three patients with testicular seminomas, spermatozoa were stored before radiotherapy and in this group, two pregnancies resulted. In one case, AIH was performed because of vaginismus after 12 years of marriage. A pregnancy resulted and the patient had a normal vaginal delivery and is pregnant a second time with normal coitus.

In the eighteen cases where the mucus was consistently found to be an impenetrable barrier to spermatozoa (negative sperm penetration tests), the cervix was bypassed by introducing spermatozoa and buffer into the uterine

Table 2. Results of AIH when semen analysis showed oligospermia

<i>Specialist referral</i>	<i>Indication</i>	<i>No.</i>	<i>No. of inseminations/cycle</i>	<i>Result</i>	<i>% success</i>
Infertility clinic	Low grade oligospermia ($< 10 \times 10^6$ sperm./ml)	8	6	3 pregnant*	38%
Infertility clinic	High grade oligospermia ($< 20 \times 10^6$ sperm./ml)	12	3	8 pregnant†	66%
Total		20	4.5	11 pregnant	55%

* There were two abortions.

† There were two abortions.

Table 3. Number of cycles to conception following AIH

	Months								
	1	2	3	4	5	6	7	8	9
No. pregnant	6	7	9	5	2	1	—	—	1
No. of inseminations /cycle	2	3	4.5	2.5	3.0	3.0	3.0	3.0	2.0
Proportion (%)	19%	23%	28%	18%	6%	3%	0	0	1%

TEXT-FIG. 1. A comparison of the percentage of pregnancy rates following AIH on the basis of ovulation timed either by injection of Premarin or by changes in basal body temperature and cervical mucus. Open columns: i.v. Premarin, 20 mg; shaded columns: control.

cavity. In this group, thirteen pregnancies resulted (70%) although two cases aborted at 8 and 10 weeks' gestation, respectively.

In Table 2, the results of intrauterine AIH in twenty instances of oligospermia are shown. An overall pregnancy rate of 55% resulted, but four women aborted in the first trimester of pregnancy. In three instances, the sperm count was very low ($<5 \times 10^6$). In this group, two to three samples were pooled resulting in an increased sperm density of 50%. The pooled samples were then inseminated as described.

Table 3 gives the number of inseminations per cycle in forty women, with ovulation timing based on basal body temperature and cervical mucus data only. Text-figure 1 gives a comparison of ovulation timing using intravenous Premarin and basal body temperature and cervical mucus.

Complications

Out of a total of 400 intrauterine inseminations, only three women were admitted to hospital because of the development of cramp-like pains. However, 15% of women experienced some lower abdominal discomfort which was only admitted to the author on questioning. No other complications occurred.

DISCUSSION

Accurate estimation of the optimal time of ovulation is of paramount importance in achieving conception when using an intrauterine insemination technique. It is now accepted that the optimal time for insemination is the day of ovulation, or 1 to 2 days before ovulation (Behrman, 1959). Foldes (1972) has reported that intravenous conjugated oestrogen (Premarin) greatly increases the success rate of AIH. The intravenous injection of oestrogen suppresses full secretion by 'feedback' and induces LH secretion by increasing the oestrogen 'surge'. The number of inseminations/cycle was greatly reduced and the accuracy of prediction of ovulation was increased as indicated by the pregnancy rate into the group of ten patients with normal sperm counts who were randomly selected for treatment with Premarin (Text-fig. 1).

It is now recognized by numerous workers (e.g. Faundes, Croxatto, Medel & Vera, 1971) that of the many millions of spermatozoa deposited in the vagina after normal coitus only thousands of spermatozoa can be recovered from the uterine cavity. For this reason, it seemed logical to suppose that relatively low sperm counts inseminated into the uterine cavity would give numbers equivalent to those reaching the uterine cavity after normal coitus, provided motility is good. Objections have been raised to intrauterine insemination because of the complication of violent cramps, as well as the risk of intrauterine infection and chemical salpingitis (Carruthers, 1970; Warner, 1971). For this reason, it is important that the pH of the buffer should be 7.2 to 7.4 and streptomycin should be added to overcome any possible infection.

Another factor to be considered is that intrauterine insemination may overcome any cervical factors such as spermagglutinins or antisperm antibodies present in the cervical mucus (Parrish & Ward, 1968).

Liquid nitrogen is now the universally accepted refrigerant for the storage of

frozen semen. Semen in 'straws' has been found to freeze more evenly, presumably because the temperature changes are evenly spread throughout the diluted semen and better recovery rates of motile spermatozoa have been recorded. Another advantage of the straw technique is its ability to withstand the strain involved in freezing at very low temperatures.

It is suggested that the technique of intrauterine insemination of husband's semen has a place to play in the treatment of infertility. Complications of intrauterine AIH using stored semen and buffer solution are greatly reduced.

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