Factors that influence the outcome of the intrauterine insemination with husband's sperm

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Summary: A retrospective analysis was undertaken in 160 intrauterine insemination with husband's sperm (IUIH) cycles, performed in 45 couples. The male factor represented the main indication (80%). Women who conceived had a lower duration of infertility (4.4 years ± 3.0 vs 7.7 ± 2.98). A significantly and pardoxically lower motility (3+ and 2+) was observed in raw specimens within conceptional cycles. However in prepared specimens in conceptional cycles the percentage of motility 3+ and 2+ was significantly increased (80.6% ± 8.1 versus 70.7% ± 20.2). The most significant difference was found in regard to a better response to preparation among conceptional cycles, expressed as the percentual increase in motility 3+ and 2+ (55.6% ± 3.9 vs 41.3% ± 19.4).

Key words: Intrauterine insemination; Husband's sperm; Motility; Prognostic factors; Semen preparation.

INTRODUCTION

Intrauterine insemination with husband's sperm (IUIH) is a technique in the treatment of infertility which has been a subject of controversy for many years. The pregnancy rates have varied widely, ranging from 0% (Ho *et al.*, 1989) to 62% (Barwin, 1974) per woman and 0% (Ho *et al.*, 1989) and 17% (Dodson *et al.*, 1987) per cycle. This discrepancy is partly due to different patient selection, number of cycles, management of ovarian cycle, techniques of seminal preparation and methodology employed to express the results. In the other hand, studies on prognostic factors and seminal parameters that influence the results of IUIH have been scarce (McGovern *et al.*, 1989; Horvath *et al.*, 1989; Tredway *et al.*, 1990; Francavilla *et al.*, 1990). The purpose of this study is to analyse the differences existing among couples and cycles in which pregnancy was achieved in regard to those in which pregnancy was not obtained.

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MATERIALS

We analysed 160 IUIH cycles performed in 45 couples assisted at the Reproductive Unit of the Hospital of Cruces - Baracaldo (Vizcaya, Spain), between October 1988 and June 1989. Of these, 41 complained of primary infertility

(91.9%) and 4 of secondary infertility (8.9%). Mean infertility duration was 6.3 years ± 3.1 (SD). Mean age of the woman was 31.7 ± 3.3 (range 25-39), and mean age of the male 34.5 ± 3.5 (26-42). Only one couple had a previous child (2.2%). The main indication for IUIH was the male factor (80.0%), followed by the cervical factor (15.6%). There was a 4.4% of idiopathic infertility. Only 15.6% of the men were considered to be normal, 26,7% were diagnosed of astenozoospermia, 11.1% of oligoastenozoospermia, 37.8% of astenoteratozoospermia, and the remaining 8.9% had different diagnoses (retrograde ejaculation, immunologic infertility, hypospermia). Antisperm antibodies in plasma were systematically investigated in both women and men.

The female workup included at least blood chemistry, endometrial biopsy, plasma prolactin and progesterone, postcoital test, hysterosalpingography and usually laparoscopy. Only 48.9% of the women were considered to be without pathology. The following pathologies were found: ovulatory dysfunction (26.7%), tubal factor (unilateral or relative bilateral) (11.1%), endometriosis (20.0%), uterine factor (11.1%), immunological factor (2.2%). Seminal preparation was performed with sperm washing (Tredway *et al.*, 1990) (11.1%), swim-up (Arny & Quagliarello, 1987) (69.5%) and fractioned swim-up (Matorras *et al.*, 1991) (19.3%). The medium used for sperm preparation was Inra Menezo B2 (Bio Merieux, France). Specimens being normal or with mild or moderate abnormalities were prepared with swim-up, whereas those with severe abnormalities were subjected to washing or fractioned washing. The male factor was considered of the susceptible to IUIH where, though some of the parameters of the seminogram proved subnormal according to World Health Organization (WHO) standards (1987), it was possible to obtain at least 1,500,000 motile sperm/cc, after semen preparation with any of the aforementioned methods. The first seminal study included WHO standards (1987), eosine test (Eliasson, 1977) and hypo-osmotic swelling test (Jeyendran *et al.*, 1984). Motility was analysed subjectively: 3+ corresponded to lineal progression, 2+ to no-lineal progression and 1+ to « in situ » motility.

The ovarian stimulation was performed with human menopausal gonadotropin (hMG) and human chorionic gonadotropin (hCG) in 74.4% of cycles, whereas the remaining 25.6% followed different regimens (6.2% clomiphene citrate plus hCG, 16.7% clomiphene citrate and hMG plus hCG, 2.5% spontaneous cycle plus hCG). Monitoring ovarian stimulation was performed with plasmatic estradiol (E_2) and echography. A single insemination was performed per cycle with 0.3-0.5 cc, 24-36 hours after the administration of 5,000 units of hCG. The insemination was performed by a staff physician, by means of a polyethylene catheter (Frydman catheter, Imesa, Barcelona, Spain), with the woman in lithotomy position. The catheter was gently inserted into the uterine cavity to within a few millimeters of its top.

The contents of the syringe were slowly injected over 1 minute. In cases of cervical stenosis a tenaculum was applied. After 20 minutes of resting in the supine position, the patients reasumed normal activity. A total of 6 cycles of IUIH were performed if pregnancy had not already been obtained. The reproductive outcome of the aforementioned patients has been published recently: 9 pregnancies (8 term pregnancies and 1 abortion) were achieved (9). The pregnancy rate per woman was 20% (9/45) and the pregnancy rate per cycle 5.6% (9/160) The statistical analysis was performed by means of Student « t » test, χ^2 test and Fisher's exact test, following the standard criteria of applicability.

RESULTS

1) *Reproductive parameters* (Tab. 1).

The frequency of primary infertility was similar among women who conceived and those who did not conceive. Although a trend was observed for lower ages among the couples who conceived, there were no significant differences (mean male ages 32.62 ± 4.00 and 35.06 ± 3.63) ($p = 0.105$, $t = 1.66$). The only parameter which significantly differed was the duration of infertility (4.44 years ± 2.30 among couples who conceived versus 7.00 ± 2.98 among those who did not conceive) ($p < 0.05$, $t = 2.39$).

The frequency of the different male diagnosis was similar in conceptional and non-conceptional cycles: astenozoospermia (22.2% and 28.6%), astenoteratozoospermia (55.5% and 40.0%), retrograde ejaculation (100% -one case and 0%), oligoastenozoospermia (0 and 11.4%). Nor were there differences regarding female diagnosis: ovulatory dysfunction (22.2% and 28.6%), tubal factor (11.1% and 11.4 %), endometriosis (11.1 % and 22.8 %), uterine factor (11.1 % and 11.4 %), cervical factor (11.1 % and

Table 1. — *Reproductive parameters among couples who conceived and who did not conceive.*

	Couples who conceived %	N.	Couples who did not conceive %	N.	p	(Student t)
Primary infertility	88.9	8	88.6	31	ns	
Woman < 30 years	44.4	4	22.9	8	ns	
Male < 35 years	62.5	5	38.7	12	ns	
Normal male	11.1	1	17.1	6	ns	
Normal female	66.7	6	42.9	15	ns	
Years of infertility (± SD)	4.44±2.30		7.00±2.98		$p < 0.05$	($t = 2.39$)
Woman mean age (± SD)	30.78±3.80		32.20±3.14		ns	
Male mean age (± SD)	32.62±4.00		35.06±3.63		$p = 0.105$	($t = 1.66$)

20.0%), immunological factor (0% and 2.9%).

2) *Seminal morphology and reproductive outcome.*

There were no significant differences regarding the seminal cell morphology (% of normal forms, density of normal forms, hypo-osmotic swelling test, eosine test) studied in the cycle immediately before the beginning of IUIH. There was even a trend approaching the statistical significance to a lower total number of normal forms among the women who conceived (84.5 millions ± 43.1 versus 127.7 ± 113.7) ($p = 0.102$, $t = 1.67$).

3) *Volume, density and motility of the ejaculate* (Tab. 2).

Neither the volume of the ejaculate, the total number of sperm cells, or the density significantly differed between the two groups. Nor did the motility differ when expressed in percentages. However, when the motility was analysed by means of the number of motile sperm cells per cc, significant differences were found regarding lower values for the conceptional cycles, either in motility 2+ (12.9 millions ± 4.8 versus 18.3 ± 15.8; $p = 0.016$, $t = 2.59$), or in the sum of motility 3+ and 2+ (14.1 ± 5.0 versus 21.2 ± 22.7; $p = 0.008$, $t = 2.76$). However,

Table 2. — *Characteristics of the raw specimen in conceptional and non-conceptional cycles.*

	Conception cycles Mean ± SD	Non-conception cycles Mean ± SD	p	
Volume of the ejaculate (cc)	3.13+ 2.04	2.86± 1.90	ns	
Density (millions spermatozoa/cc)	54.4 ±18.8	59.6 ± 33.1	ns	
Total number (million)	157.6 ±93.6	161.2 ±116.8	ns	
Motility 3+ (%)	2.2 ± 3.6	2.8 ± 7.5	ns	
Motility 2+ (%)	23.9 ± 4.9	26.9 ± 11.7	ns	
Motility 3+ and 2+ (%)	26.1 ± 6.5	29.7 ± 14.8	ns	
Motility 3+ (Million/cc)	1.2 ± 1.8	2.9 ± 12.0	ns	
Motility 2+ (Million/cc)	12.9 ± 4.8	18.3 ± 15.8	0.016	($t = 2.59$)
Motility 3+ and 2+ (Million/cc)	14.1 ± 5.0	21.2 ± 22.7	0.008	($t = 2.76$)
Total motility 3+ (Million)	1.6 ± 2.8	6.6 ± 34.8	ns	
Total motility 2+ (Million)	37.2 ±23.4	45.7 ± 42.6	ns	
Total motility 3+ and 2+ (Million)	38.7 ±22.1	51.9 ± 60.6	ns	

Table 3. — *Characteristics of prepared specimens.*

	Conception cycles Mean ± SD	Non-conception cycles Mean ± SD	p
Postoperation volume (cc)	0.49± 0.03	0.48± 0.10	ns
Percent of motility 3+	20.0 ± 9.7	21.5 ±11.6	ns
Percent of motility 2+	60.6 ±11.6	49.3 ±15.9	< 0.05 ($t = 2.07$)
Percent of motility 3+ and 2+	80.6 ± 8.1	70.7 ±20.2	< 0.01 ($t = 3.04$)
Density of sperm (Million/cc)	45 ±22.4	45.8 ±28.3	ns
Density motile 3+ (M/cc)	9.9 ± 8.0	10.3 ± 9.6	ns
Density motile 2+ (M/cc)	26.3 ±12.1	22.2 ±14.6	ns
Density motile 3+ and 2+ (M/cc)	36.2 ±18.3	32.4 ±22.1	ns

when the motility was analysed in terms of total values, again there were no differences.

4) *Method of seminal preparation.*

With the swim-up preparation a 7.08% fecundity rate per cycle was obtained (8/113), versus a 3.57 % with fractioned swim-up (1/28) and no pregnancy with sperm washing (0/19). The differences were not of statistical significance.

5) *Characteristics of prepared specimen* (Tab. 3).

Among conceptional cycles the following motility groups were significantly increased when their percentage were considered: motility 3+ and 2+ (80.6% ± 8.1 versus 70.7% ± 20.2; $p < 0.01$, $t = 3.04$) and motility 2+ (60.6% ± 11.6 versus 49.3% ± 15.9; $p < 0.05$, $t = 2.07$). However, when motility was analysed in terms of density per cc, there were no differences.

6) *Seminal amelioration with preparation* (Tab. 4).

Among conceptional cycles there was a better response to preparation, expressed both as the percentual increase in the percentage of motility 3 + and 2 + (55.6% ± 3.9 vs 41.3 ± 19.4), the differences being highly significant ($p < 0.0001$, $t = 6.58$). The increment in the precent of motility 2+ was also higher in conceptional cycles (37.8% ± 9.7 versus 22.7% ± 15.7) ($p < 0.01$, $t = 2.83$).

7) *Management of ovarian cycle.*

The majority of ovarian cycles were stimulated with hMG and hCG. The other protocols included few cases, precluding their comparison. There were no differences in conceptional and non conceptional cycles in hMG ampules administered (14.4 ± 6.9 vs 15.1 ± 7.5), nor were there differences in E_2 levels (1224 pg/ml ± 815 vs 1012 ± 583), the number of follicles > 16 mm (2 ± 1.5 vs 2.6 ± 1.8), their maximal diameter (18.9

Table 4. — *Increase in motility after semen preparation.*

	Conception cycles Mean ± SD	Non-conception cycles Mean ± SD	p
Inc. density (million sperm/cc)	−17.7 ± 26.9	−10.4 ± 50.1	ns
Inc. motility 3+ (%)	17.8 ± 11.5	18.8 ± 12.4	ns
Inc. motility 2+ (%)	37.8 ± 9.7	22.7 ± 15.7	< 0.01 ($t = 2.83$)
Inc. motility 3+ and 2+ (%)	55.6 ± 3.9	41.3 ± 19.4	< 0.0001 ($t = 6.58$)

mm ± 2.4 vs 19.1 ± 3.8), or in the day in which the IUIH was performed (12.8 ± 1.2 vs 13.1 ± 1.4).

DISCUSSION

IUIH is a controversial technique. In a recent review of 34 studies about IUIH including 8732 cycles and 2908 women, a mean pregnancy rate of 19.8% per woman and 6.6% per cycle were found (Matorras *et al.*, 1991). In our experience there was a 20.0% pregnancy rate per woman and a 5.6% per cycle, 8.5 times greater than in non-IUIH non-stimulated controls (Matorras *et al.*, 1991) ([9]). Pregnancy rates reported by the different authors vary widely, ranging from 0% (Ho *et al.*, 1989) to 62% (Barwin, 1974) per 1974) per woman and 0% (Ho *et al.*, 1989) and 17% (Dodson *et al.*, 1987) per cycle. These remarkable differences are due to the diversity in patient selection criteria, ovarian cycle management and monitoring, number of cycles performed, number of inseminations per cycle, technique of seminal preparation and methodology employed in reporting results.

On the other hand, prognostic factors for IUIH have been little studied (Mc Govern *et al.*, 1989; Horvath *et al.*, 1989; Tredway *et al.*, 1990; Francavilla *et al.*, 1990). In our experience, although the reduced number of pregnancies analysed make some type of alpha- error possible, a number of parameters were found to be different in regard to the achievement of pregnancy. Concerning the personal history, a lower duration of infertility (4.4 years vs 7.0) was the only significant factor associated with pregnancy. This fact is consistent with the well known generally worse prognosis of infertility as its duration increases (Kliger, 1984), although in two previous reports it was not demonstrated in IUIH (McGovern *et al.*, 1989; Horvath *et al.*, 1989). On the other hand a non-significant trend to lower ages among the couples who conceived was observed, which is also consistent with the general infertility prognosis. Although Francavilla *et al.* (1990) reported a better prognosis in IUIH with normal morphology >50%, in our study the morphology was close to 50% both among couples who conceived and in those who did not conceive.

Regarding the characteristics of the ejaculate, we found in conceptional cycles paradoxically lower values of motility, when expressed in density. Both the motility 2+ (12.9 millions/cc vs 18.3), and the sum of motility 3+ and 2+ (14.1 millions/cc vs 21.2) were significantly lower in conceptional cycles. In the literature there are some reports regarding lower values in the original number of motile sperm in pregnancy cycles or in the percentage of motile sperm cells (McGovern *et al.*, 1989; Horvath *et al.*, 1989; Tredway *et al.*, 1990), but the statistical analysis was either not performed (McGovern *et al.*, 1989) or lacked significance (Horvath *et al.*, 1989; Tredway *et al.*, 1990). Only Francavilla *et al.* (1990) reported better motile sperm count among couples conceiving, but their study included a high percentage of oligozoospermia, which was not included in our work.

One can speculate, in some cases, on some undetected chemical or immunological factor that impairs motility, which may be eliminated with preparation. However it could also be a spurious finding, or perphaps the « worse » ejaculates were subjected to a more accurate preparation: in any case this finding needs further investigation. Moreover, it must be taken into account that the aforementioned differences were not detected when considering either percentages of motility or total number of cells with each kind of motility. On the contrary, McGovern *et al.* (1989), although reporting a trend towards a low number in the original motile sperm, found that pre-wash motility, consistently ≥ 30% or better if ≥ 70%, was a good prognostic factor.

However, taking into account that in our study both in the conceptional group and in the non-conceptional group mean motility 3+ and 2+ was lower than 30%, this aspect could not be analysed. Our results are comparable with those of Hoing *et al.* (1986) in that mean motility was similar in conceptional and non-conceptional cycles.

More consistent was the study of the motility after preparation. In conceptional cycles the percentage of motility 3+ and 2+ (80.6% vs 70.7%) and of motility 2+ (60.6% vs 49.3%) were significantly increased. Previously it was reported that once a motility of 40% was reached, higher values did not improve cycle fecundity (Horvath, 1989). However, our results are similar to those of Arny and Quagliarello (1987) in poor postcoital tests (excluding male factors), where it was found that a post-swim-up motility >79% was a good prognostic factor. Our work demonstrates that there is a mechanism dose-response in IUIH, arguing in favour of the effectiveness of the procedure.

Another remarkable finding was the better response to preparation in conceptional cycles, expressed as the percentual increase in motility 3+ and 2+ (55.6% vs 41.3%). Although a trend to superior values in pregnancy cycles had been reported, it lacked statistical significance (McKGovern *et al.*, 1989). Taking into account that the response to preparation was the most significant parameter among those we analysed the consideration of such a factor could be suggested when establishing the indication of IUIH. However, the great variability from one cycle to another reduces its clinical usefulness.

Other parameters described as prognostic factors in the literature, such as gonadotropin stimulation (Kemman *et al.*, 1987), seminal preparation (Blumenfeld *et al.*, 1989; Pardo *et al.*, 1988), indications for cervical factor or poor postcoital test (McGovern *et al.*, 1989; Hull *et al.*, 1986) were not demonstrated in our study. This is probably due to the limited number of study cases and to the retrospective nature of our work. This is also the probable explanation as to why the presence of pathology in the woman was not correlated with a significantly poor prognosis.

To sum up, the IUIH success rate is associated, firstly with a better response of the motility to semen preparation, and secondly to a higher prepared specimen motility. However the range of the variability was wide, precluding their use as indicatiors for IUIH or not. On the other hand, the better motilities associated with conceptional cycles speaks in favour of the real efficacy of the IUIH.

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