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ORIGINAL ARTICLE

Factors Leading to Pregnancies in Stimulated Intrauterine Insemination Cycles and the Use of Consecutive Ejaculations Within a Small Clinic Environment

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Abstract

Introduction Understanding and improving IUI pregnancy rates has enormous global appeal and application. This pilot study goes one step further by utilising consecutive ejaculates from men with oligozoospermia and comparing with normozoospermic male group.

Materials and Methods A retrospective analysis was performed on 117 IUI-stimulated treatment cycles in a small fertility clinic in North Middlesex University Hospitals Trust, UK, within a NHS setting. Risks of OHSS and multiple births are carefully controlled.

Results In our cohort, several factors are associated with positive IUI pregnancies and these were: age of the woman, inseminating with ≥5 total progressive motile sperm; having ≥50 % Grade A sperm progression and having ≥1

follicle achieved with a realistic hMG dosage, hCG trigger and IUI of 29.7 h (2.5–38.4 h), with an endometrial thickness of 10.7 mm (6.6–13.4 mm). Bifollicular presence in at least half the cases along with hMG protocols added usefully to the pregnancy outcomes.

Conclusions The pregnancy rates per cycle were 19 and 23 % in the consecutive ejaculates and non-consecutive ejaculate groups, respectively, $P = 0.59$. For the whole cohort, the pregnancy rate was 20.51 % per cycle and 33.8 % per women. This approach if validated with large RCT will have universally beneficial effects.

Keywords Intrauterine insemination · Gonadotrophin · Male factor infertility · Consecutive ejaculates · Total progressive motile sperm

Introduction

Since the first paper on intrauterine insemination (IUI) was published in 1962 by Cohen [1], there has been an astonishing lapse in progress detailing how to improving clinical pregnancy rates such as those witnessed with IVF/ICSI practices. Over 70 million couples worldwide require fertility treatment, and for most only low-cost and simple first-line treatment options are available [2, 3] usually performed in local clinics. In order to improve pregnancy outcome, we need an in depth analysis of factors which may lead to a successful pregnancy in the local cohort of patients. A systematic review reported that further research through well designed studies was needed to unravel the determinants of success for IUI [4]. Despite several leads on the contributing factors for IUI such as woman's age, duration of infertility, follicle numbers, endometrial thickness, BMI, number of cycles of IUI and catheter types [5–7], ovulation induction, timing of insemination and total motile sperm numbers for IUI, none of the information has been presented in a way to serve as guidance on improving IUI pregnancy rates. Studies have shown that IUI is of little therapeutic benefit unless combined with ovulation induction [8, 9] and IUI derives most of its therapeutic benefit from multifollicular development. Similarly, others have found that ovulation induction with gonadotrophins significantly improves for example donor insemination success [10]. Equally, on male factors, numerous detailed reports exist on sperm parameters, but practitioners are limited on improving this component. Progressive motility and number of motile sperm in the inseminate are recognised to be of prognostic value [11–13].

Recent reports support the effectiveness of IUI procedure [14, 15] and ask whether traditional IVF with conventional ovarian stimulation, single embryo transfer and subsequent cryo-cycles (IVF), or IVF in the modified natural cycle (IVF-MNC), or stimulated IUI (IUI-COH) is to be preferred from a cost-effectiveness point of view as a first-line treatment in couples with unexplained subfertility and an unfavourable prognosis on natural conception. They found that both IVF strategies are significantly more expensive when compared to IUI-COH, without being significantly more effective. When comparing between IVF-MNC and IUI-COH, the latter is the dominant strategy. The cost-effectiveness of IUI over IVF is confirmed when treatment occurs above a pre-wash total motile sperm count (TMSC) of 3 million [16], thereby highlighting the need for more motile sperm for IUI effectiveness. A recent report confirms that consecutive ejaculates in subfertile males provide better sperm quality in the consecutive ejaculate [17] with better sperm motility and progression in the consecutive ejaculate, therefore, the limitation of motile sperm numbers has the potential to be overcome by this strategy. Men with oligozoospermia provided consecutive ejaculates. The situation leads onto an interesting question as to whether men with oligozoospermia when providing a consecutive ejaculate narrow the difference with normozoospermia males when being treated with their partners for IUI.

The aim of this retrospective pilot study was to analyse factors associated with a positive IUI pregnancy along with whether combining consecutive ejaculates gives similar pregnancy rates for oligozoospermia patients compared to one ejaculate for normospermic patients within our local cohort. We recognise the limitation in quantifying the magnitude of differences in various factors contributing towards a positive pregnancy within this pilot study, but anticipate this to be a precursor towards a prospective RCT study.

Materials and Methods

Subfertility patients were treated for IUI at the North Middlesex University Hospital, UK, in the Reproductive Medicine Unit (RMU). Patients were managed by a nurse led specialist clinic for baseline investigations, counselling and consenting, ovulation monitoring, injection teaching. Regular clinic meetings were established to monitor pregnancy outcomes and alter practices to improve our pregnancy outcome. Data from January to September 2014 on 71 women receiving 117 IUI cycles were retrospectively analysed in detail and reported.

For Females

Nulliparous women in a heterosexual relationship with ≥2 years history of subfertility were offered 6 cycles of IUI. The patient telephoned the centre on (or soon after) day 1

of the onset of her period to make an appointment for her first ultrasound scan (baseline scan days 3–5 of the cycle to check endometrial thickness and ovaries).

Following the scan on days 3, 4, and 5, the patient administered the first dose of the gonadotrophins under the nurse's supervision. After four doses of menopur, ultrasound scan was performed to monitor follicular growth and then the gonadotropin dosage was adjusted to minimise multiple follicles. The standard dose of gonadotrophin (Menopur, Ferring) was 150 iu on alternate days. The patient was provided with information on the amount and time of each administration of gonadotrophins. The first ultrasound scan was booked around 7–8 days later. Further scans were arranged depending on the response (endometrial thickness and follicles size) at each visit as well as the gonadotrophin′s dose.

When the leading follicle(s) was at 17–18 mm or more, the patient was prescribed hCG (Pregnyl/Gonasi) 5000 iu and an appointment was made for the IUI to take place 24–40 h after the injection. If there was any evidence of ovulation (corpus luteum plus free fluid in the pelvis), then the patient had insemination on the same day or she would have been advised for timed sexual intercourse. The cycle was abandoned if there was evidence of OHSS, or having 4 or more leading follicles, or there was no response in spite of increasing the gonadotrophin dose. Abandoned cycles were discussed in house beforehand, as were those patients receiving IUI with 2–3 follicles. IUI took place soon after samples preparation followed by bed rest for 15 minutes. Post-insemination, all IUI patients were prescribed Cyclogest 400 mg twice a day for 14 days and advised to take a pregnancy test after the 14 days. Pregnancy was confirmed by the detection of a foetal heart.

For Males

A dedicated room next to the laboratory was used by men to provide the semen sample, and a fresh sample was processed immediately after liquefaction. Before IUI was considered by the nurse/clinician, semen profiling was performed with a view to gaining $\geq$5 million TPMS for insemination. In subfertile male patients with oligozoospermia and where the initial 'total progressive motile sperm count' (TPMS) was $\leq$10 million before processing, a 'consecutive ejaculate' was requested to supplement the initial ejaculate. The patients were counselled for the need to work towards achieving a $\geq$5 million TPMS for the purpose of IUI, and this motivated them to provide the consecutive ejaculate.

In at least half the male cases, this entailed requesting a 'consecutive ejaculate' (second ejaculate) produced within half an hour of the first, which when combined with the first ejaculate allowed the threshold of TPMS to be brought above $\geq$5 million in most cases. Failure to reach this threshold did not lead to a rejection of a planned IUI unless all sperm were immotile or the number of leading follicles exceeded three. There was no additional cost to obtaining and processing a 'consecutive ejaculate' other than extra effort and time management imposed on the male patient and the laboratory. Production of a 'consecutive ejaculate' was usually unproblematic with most men. Sperm preparation utilised gradient method using Pureception (Sage, USA) and Quinn's Sperm washing medium (Sage, USA). Where 'first' and 'consecutive ejaculates' were involved, the ejaculates were pooled and processed, while the pellet was combined to make up to 1-ml Quinn's sperm medium for IUI. Although the WHO 2010 [18] compounded the 'Grade A + B' movement for 'progressive sperm', we retained the original grading for the purpose of critical analyses of our data in line with the ABA recommendation [19].

Progression was classified as: Grade A (3): rapid progressive movement. At least 25 μm/s at 37 °C (25 μm is approximately equal to 5 head length or half a tail length). Grade B (2): progressive motile with moderate to poor progression. Grade C (1): twitching sperm with minimal forward progression. Grade D (0): non-progressive motility. $<$5 μm/s at 37 °C.

The final insemination report detailed the TPMS and exact age of the woman on the day of insemination, and an Excel spreadsheet was used to monitor IUI and its outcomes.

Excluded from this report were women receiving donor sperm, men or women with history of cancers, tubal disease or occlusion detected during baseline HSG scan, reversal of sterilisation and multiparous women.

The Reproductive Medicine Unit participates fully with the external quality assessment by the UK NEQAS, Sub-Fertility Laboratory, Saint Mary's Hospital, Manchester, UK.

Statistical Methods

This was a retrospective cohort study. The primary outcome was comparison of pregnancy rates in women who were inseminated with consecutive ejaculates versus the standard single ejaculate insemination method. The secondary outcome was to investigate and describe any factors that were associated with a positive pregnancy. Cancelled cycle due to ovarian stimulation is regarded as cycle started and included in the overall calculations. The analysis of the data was carried out using Stata IC 13 (StataCorp, 4905 Lakeway Drive, College Station, Texas 77845, USA). The data are presented in means and standard deviations, medians and inter-quartile ranges, or percentages. Non-parametric methods such as Chi-square and Fisher's exact were used to test any associations where appropriate. A P value of $\leq$0.05 was considered to be significant.

Results

A total of 117 IUI treatment cycles were performed on 71 women, and 24 clinical pregnancies were obtained. The pregnancy rate is 20.51 % per cycle and 33.8 % per women on our cohort. Male factors were significantly inferior in the consecutive ejaculates group at baseline and prior to mixing with the second sample, as given in Table 1. Other baseline characteristics were similar between the two groups. Administering the consecutive ejaculate improved all the male factors as detailed in Table 1. This resulted in similar pregnancy rates in both groups despite the worse baseline parameters for the consecutive ejaculates group, $P = 0.59$. The TPMS was 13.5 million in the consecutive ejaculates group and 15 million the in non-consecutive group, indicating that male factors

Table 1 Baseline characteristics in the study cohort

	Consecutive ejaculates					Non-Consecutive ejaculates					*P*
	Mean	SD	Median	Min	Max	Mean	SD	Median	Min	Max	
Female age (years)	33.06	3.60	32.7	25.7	38.5	33.84	3.50	34.15	27.9	42.3	0.37
Partner's age (years)	35.26	4.17	35.11	26.32	48.46	37.47	6.01	36.53	28.07	51.89	0.06
Sperm count	29.26	17.95	26	3	84	34.44	13.88	33	9	75	0.01
TMC	15.27	7.56	15.57	1	32.8	13.53	8.79	12.8	1.75	41.6	0.19
Progressive motility %	37.97	8.10	40	20	60	41.25	6.06	40	30	50	0.006
Sperm progression grade	1.75	0.29	2	1	2	1.91	0.27	2	1	2.5	0.023
Abnormal sperm %	95.13	1.91	95	91	98	94.15	1.74	94	92	98	0.003
Normal sperm %	4.87	1.91	5	2	9	5.85	1.74	6	2	8	0.003
Volume (ml)	4.07	1.82	4	0.55	9	2.48	1.05	2.5	0.4	6	0.000
Prep count	35.68	21.68	36	5	104	38.96	18.81	40	4	82	0.32
Prep progressive motility %	73.62	8.04	80	50	90	77.08	7.64	80	50	90	0.02
Prep sperm progression grade[a]	2.42	0.40	2.5	1.5	3	2.57	0.40	2.5	1	3	0.02
Follicle numbers	1.10	0.43	1	1	3	1.21	0.54	1	1	3	0.12
Endometrial thickness (mm)	10.12	1.71	10.3	6.6	12.4	11.33	1.93	11.8	6.9	13.4	0.06
BMI	26.61	1.49	27	22.5	29	26.49	1.44	27	22.5	27	0.48

Progressive motility and prep progressive motility refer to motility in neat fresh sample and in processed samples, respectively

[a] Progression grades: Grade A: (assigned 3); Grade B (assigned 2); Grade C (assigned 1); non-progressive motility (assigned 0)

Table 2 Characteristics of the pregnant and non-pregnant groups

	Non-pregnant group					Pregnant group				
	Mean	SD	Median	Min	Max	Mean	SD	Median	Min	Max
Female age (years)	33.31	3.64	33.7	25.7	42.3	33.66	3.32	33.25	28.5	39.7
Partner's age (years)	35.65	4.88	35.32	26.32	51.81	38.15	5.57	37.02	28.11	51.89
Sperm count	32.11	16.17	28	3	83	28.58	17.99	27.5	5	84
Progressive motility %	39.25	7.66	40	20	60	39.58	6.90	40	30	60
Sperm progression grade	1.82	0.30	2	1	2.5	1.77	0.25	2	1.5	2
Abnormal sperm %	94.67	1.89	94	91	98	94.96	1.94	95	91	98
Normal sperm %	5.33	1.89	6	2	9	5.04	1.94	5	2	9
Volume (ml)	3.47	1.75	3.2	0.4	9	3.23	1.70	2.75	0.7	6.5
Prep count	37.74	19.41	39	4	82	34.25	24.66	25.5	10	104
Prep progressive motility %	74.84	8.52	80	50	90	75.83	5.84	80	60	80
Prep sperm progression grade[a]	2.46	0.40	2.5	1	3	2.56	0.43	2.5	2	3
Follicle numbers	1.00	0.00	1	1	1	1.71	0.86	1	1	3
Endometrial thickness (mm)	–	–	–	–	–	10.68	1.88	11	6.6	13.4
BMI	26.54	1.48	27	22.5	29	26.67	1.45	27	22.5	29

Progressive motility and prep progressive motility refer to motility in neat fresh sample and in processed samples, respectively

[a] Progression grades: Grade A: (assigned 3); Grade B (assigned 2); Grade C (assigned 1); non-progressive motility (assigned 0)

Table 3 Pregnancy rates in consecutive and single ejaculates

	No pregnancy		Pregnancy	
Single	37	77 %	11	23 %
Consecutive	56	81 %	13	19 %
Overall	93	79.50 %	24	20.50 %

Pearson $\chi^2 = 0.2884$, $P = 0.591$

detrimental to a successful pregnancy were normalised to the level of the comparator group (see Table 1).

The characteristics of the pregnant and non-pregnant groups are given in Table 2. For the pregnant cohort, the time lapse between HCG trigger and insemination was a median of 28.8 h (IQR 25.8–35.4 h). The endometrial thickness of 10.7 mm (SD 1.8 mm) was recorded 28.8 h (median, IQR 25.8–35.4 h) prior to hCG trigger. Ovulation induction in the pregnant group yielded a mean of 1.71 (SD 0.86) leading follicles per patient, and six women had three leading follicles (25 % of cohort), while five women had two leading follicles (20.8 % of cohort) and 13 unifollicular women (54.2 % of cohort). No twin or triplets were formed, and no foetal reduction or OHSS was recorded. Our offer of six-cycle treatment was justified with pregnancies in all cycles.

In the pregnant group, 87.5 % of the inseminations were performed with ≥5 million TPMS where consecutive ejaculates crucially contributed. 'Consecutive ejaculates' were associated with 54 % of the pregnant cohort, and the association was in 60 % (12/20) of women aged <37 years and in 25 % (1/4) in women aged >37 years. The lowest TPMS in our cohort for pregnancy was 3.5 million and 1 million in the non-pregnant group. High sperm counts >20 million TPMS was not detrimental to a woman's chance of achieving a pregnancy. Of the total pregnancies associated with TPMS, 41.8 % ($n = 10$) resulted from sperm progression of Grade A (100 %); 29.1 % ($n = 7$) with Grade A + B (proportion of 70:30); and 29.1 % ($n = 7$) with Grade A + B (proportion of 50:50) sperm progression. No pregnancies occurred when the B grade sperm proportion in the inseminate increased above 50 %. Women aged <37 years (25.7–36.9) had pregnancy rates as follows: 20.8 % per cycle and 33.5 % of cohort pregnant (96 cycles, 59 women and 20 pregnancies). Women aged >37 years had pregnancy rates as follows: 9.3 % per cycle and 28.6 % of cohort pregnant (43 cycles, 14 women and four pregnancies). BMI for all women was <30.

Discussion

The main results show that several factors were responsible for a pregnancy outcome and male factor problem detrimental to a successful pregnancy has the potential to be overcome by using consecutive ejaculates. The IUI pregnancy rate was 20.51 % per cycle and 32.9 % per women within our cohort. Factors associated with successful IUI pregnancies were age of woman <37 years, ≥5 million TPMS with at least 50 % Grade A sperm progression, number of follicles and 150 iu hMG, with IUI occurring 29.7 h (2.5–38.4 h) post-hCG trigger. A realistic dose of hMG ovulation induction protocol is essential. In the pregnant group, 87.5 % of the inseminations were performed with >5 million TPMS assisted with consecutive ejaculates to achieve this figure. 'Consecutive ejaculates' were associated with 54 % of the pregnant cohort. Although aiming for >5 million TPMS, IUI appears to require a minimum of 3 million TPMS for a realistic chance of pregnancy in IUI cycles, while above 20 million TPMS for IUI are not detrimental for a woman's chance to achieve a pregnancy. Ovulation induction in the pregnant group yielded a mean of 1.71 leading follicles per patient. Approximately half the pregnant cohort had 2–3 leading follicles. Inseminating with 2–3 follicles seems an acceptable risk of multiple births for an IUI procedure given that we had no multiple births or OHSS, but continue vigilance with regards to risks. No pregnancies occurred when the A grade sperm progression in the preparations fell below 50 % or conversely where B grade sperm exceeded 50 % in the sample for insemination. Sperm progression therefore had a positive association with pregnancies of where 41.8 % of pregnancies were associated TPMS with Grade A (100 %) and none of the pregnancies in this cohort having >50 % B grade sperm. Grades A and B sperm movement have now been compounded as 'progressive sperm only' [19]. Retaining the grading for the purpose of our critical analyses showed a trend in pregnancies being associated with better linear sperm progression, and this is recognised elsewhere [13, 20, 21]. Inseminations were performed soon after freshly produced semen is prepared requiring minimal waiting time, and this factor is reported [22]. Perhaps the most important finding of our study was that it was possible to achieve an equitable status for pregnancy success between subfertile oligozoospermia and normozoospermia groups male partners, by supplementing TPMS using a 'consecutive ejaculate' with the former group. This fact has novelty value in IUI practice.

The first major change in our IUI practice over 5 years was to shift away from clomiphene to hMG protocols and secondly to incorporate 'consecutive ejaculates' for men with oligozoospermia, especially where the initial TPMS was ≤10 million. The consecutive ejaculate obtained within 30 min of the first ejaculate was retrieved for motile sperm and combined for IUI. There was no delay for IUI post-samples preparation which was followed by bed rest for 15-min post-IUI. We had increased the hMG dosage to 150 iu while having a strict monitoring and cancellation policy for higher-order pregnancies and OHSS.

Our poor experience in earlier years with clomiphene cycles yielded low pregnancy rates of around 7 % per cycle. Ovulation induction protocols making extensive use of clomiphene since the mid-1960s had never optimised, and this has led to poor pregnancy rates in IUI. The endometrial thickness tends to be much poorer than in hMG-stimulated cycles. Recent data suggest that the pregnancy-related diameter of the leading follicle in CC cycles is significantly larger than that in gonadotropin cycles and the best time for hCG trigger in the CC cycle is when the leading follicle reaches 20 mm [23]. It is important to reflect on the differences between these regimes. [24, 25]. Clomiphene an anti-oestrogen is a selective oestrogen receptor modulator (SERM), a nonsteroidal oestrogen that binds to the oestrogen receptors at multiple sites throughout the reproductive tract and can act as an oestrogen agonist or as an antagonist. Clomiphene binds to oestrogen receptors in the hypothalamus, inhibiting negative feedback of oestrogen on gonadotrophin release. It is unclear to what extent in particular clomiphene interferes with the functional properties of sperm given that human sperm expresses the oestrogen receptors [26]. Gonadotrophins are glycoprotein hormones that can be extracted from urine of menopausal women or can be manufactured in recombinant variants. They stimulate follicular growth by acting directly on ovarian FSH receptors and have no anti-oestrogenic effect on cervical mucus or endometrium-like clomiphene. A recent report confirms that ovarian stimulation with low-dose hMG was superior to CC in IUI cycles with respect to clinical pregnancy rate [27], thereby justifying using gonadotropin regime.

Reviewing IUI successes is complex given the lack of standardisation in interpreting semen analysis results; TMSC (different from TPMS) referred to ejaculates while others processed samples; confounding factors such as the duration of infertility and female age, methods of sperm preparation and the diverse causes of infertility included in such studies make reliable conclusions hard to come by [4, 21]. When it came to male factor consideration, attaining 5 million motile sperm threshold for IUI is recommended [21, 28], while there is no consensus on a lower limit of semen quality at which one would advocate IUI [29];the systematic review confirms favourable correlation with IUI success in the range of 5–10 million [30].

Therefore, the second major change to our protocol was to obtain a consecutive ejaculate to boost the male factor deficit for subfertile men with oligozoospermia, by supplementing the initial ejaculate where the initial TPMS was $\leq$10 million. The consecutive ejaculate was produced within 30 min of the first ejaculate, and this was the shortest abstinence times on record. Consecutive ejaculates were also associated with better progressive sperm. By combining the two consecutive ejaculates, the IUI pregnancy rates between the oligozoospermia and normozoospermia males were similar (Table 3), and therefore the initial indication from our work suggests a route to overcome male factor obstacles in IUI procedures by applying 'consecutive ejaculates'. Consecutive ejaculates were associated with 60 % (12/20) of pregnancies in women aged <37 years and with 25 % (1/4) in women aged >37 years further suggesting that the older women cohort most probably had male partners with already reasonable sperm quality and that the age of the woman was the most likely subfertility factor.

Multiple births have been a single reason pitched against IUI, but there is no evidence whatsoever in the Cochrane review [31]. This prejudice is based on historical practices involving the irresponsible induction of high numbers of follicles during IUI procedures. For women aged <32 years, HOMP (high-order multiple pregnancy) was 6 % for three to six follicles and 20 % for seven or more follicles. For ages 32–37 years, HOMP was 5 % for three to six follicles and 12 % for seven or more follicles [5]. However, careful monitoring of follicles has now reduced the absolute rate of multiple pregnancies is 0.3 % after monofollicular and 2.8 % after multifollicular growth [32]. The risk of multiple pregnancies after stimulation of two, three and four follicles is estimated to increase by 6, 14 and 10 % [32]. The contribution made by IUI to the number of multiple pregnancies in the Netherlands was much smaller than the contribution made by IVF [33, 34]. Simply shifting IUI from unifollicular to bifollicular IUI cycles will potentially increase the chance of achieving an IUI pregnancy by 3.4-fold [6] and, along with crucial monitoring to minimise higher-order births, IUI can become an even stronger basis for first-line treatment. From our work, the presence of 2–3 leading follicles during an IUI procedure appears an acceptable risk, provided careful monitoring and strict cancellation policy is implemented.

There was insufficient evidence to determine whether there is any difference in safety and effectiveness between different methods of synchronisation and timing of ovulation and insemination [33, 34]. For our pregnant cohort, the timing of insemination was recorded as 29.7 h (mean, 2.5–38.4 h) prior to hCG trigger taking account of the restricted alternate day IUI service, and it is rather surprising that few studies were designed to find the optimal time for insemination [35]. After IUI, luteal phase support using 400 mg cyclogest was provided to all patients. It has been suggested progesterone seems to be the best option for luteal phase support, with better pregnancy results when synthetic progesterone is used [36]. In one RCT comparing low-dose hMG (75 iu) versus CC in subfertile couples treated with intrauterine insemination, IUI was performed 1 day (27–30 h) after hCG [27] giving better pregnancy rates in the hMG group.

With regard to endometrial thickness, we did not gain a clear understanding from our cohort apart from recognising they were within published figures to support pregnancies [37]. Mean endometrial thickness in patients stimulated for IVF tends to be significantly higher than in patients stimulated for IUI and normally cycling women ($P < 0.001$) [38], and pregnancy rates (PRs) are significantly higher in patients with an endometrial thickness >9 mm suggesting the need for IUI induction protocols along the lines used in IVF procedures.

Our study has its limitations for its sample size, and is a retrospective study thereby urging caution in interpreting the qualitative associations found during IUI pregnancies, until a sufficiently powered RCT is concluded. For the sample size, only univariate analyses were possible to find factors associated with a pregnancy. However, the IUI pregnancy rate of 20.51 % per cycle exceeds the UK national average of 13 % per cycle and those large cohorts' reports in European studies by almost 50 %, while indicating a threefold increase over the only RCT reported using clomiphene-induced cycles. Therefore, there is a persuasive argument to validate the study with larger RCT.

To conclude, numerous factors were associated with a positive pregnancy outcome on our IUI programme. There is indication, within the limits of our study that male factors detrimental to a successful pregnancy can be overcome with the application of consecutive ejaculates giving equitable pregnancy outcomes in women whose male partners were either oligozoospermia or normozoospermia. In other words, using combined consecutive ejaculates for patients who have sperm of <10 millions of pre-washed, there was an increase in pregnancy rate to be nearly equal to the groups with normal semen parameters. The following were also positive factors for a pregnancy: age of woman, inseminating with ≥5 million TPMS, having ≥50 % Grade A sperm progression and having ≥1 follicle achieved with a realistic hMG dosage. Bifollicular presence in at least half the cases with hMG protocols, in addition to consecutive ejaculates, helped IUI effectiveness. From 117 IUI treatment, the pregnancy rate was 20.51 % per cycle and 33.8 % per women. This approach if validated with large RCT provides a significant alteration to IUI practice with enormous benefits for patients in first-line treatment as the outcomes are towards the upper end of published outcomes.

Compliance with Ethical Standards

Conflict of interest There is no conflict of interest.

Ethical Approval The institutional review board indicated that ethical approval was not required for this study (IRAS project ID: 184567, 5th June 2015).

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