Fallopian tube sperm perfusion offers any advantage in comparison with the conventional IUI technique?: What more after 10 years of use?

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Abstract

This article summarise brifley the recent data about the Fallopian tube Sperm (FSP) with review of literature. After 10 yeas of the initial description of the FSP, there is still a great debate about its efficacy and best use versus the classic Intruterine isnemination technique (IUI).

INTRODUCTION

The demands of medical assistance in procreation have increased in recent years because of the development of various new medical techniques. The intrauterine insemination is an inexpensive, simple and tried technique, which presents a great therapeutic interest and is proposed as a first solution to infertile couples.

The FSP was first described by Kahn in 1992 [1], and has shown very encouraging results in pregnancy efficiency.

The main technical difference with the FSP method when compared to the IUI, is that the inseminate volume is increased up to 4 ml. This volume was been cosidered sufficient for bilateral passage of the inseminate throught the fallopian tubes [1] [5]. Using a variety of methods to prevent inseminate reflux from the cervix during the insemination, the intrauterine pressure is increased and the inseminate pass directly through the fallopian tubes, similar to that of hysterosalpingographies. The cervical reflux could be prevented using: pence of Allis [1] [2] [3] [4], a pediatric folley's catheter (transcervical) [5], special designed catheters [6] [7], or speculum (DNB) [8] or the FAST system [9].

Theoretically, the direct passage trough the fallopian tubes of the sperm preparation would increase the density of capacitated spermatozoids near the oocyte and the intra-peritoneal cavity and by consequence the pregnancy succes rate. Since 1992 different studies were realized with controversial results concerning the best indication for the FSP method. FSP use the same protocols of ovarian stimulation and the monoitoring of the cycle as for the IUI.

DISCUSSION

Variety of results concerning pregnancy rate with FSP versus IUI are indicated in table I.

Figure 1

Table 1: FSP total pregnancy rate, studies of 1992 to 2002

Studies 1992 to 2002	Total pregnancy rate
Kahn, et al [1]	13.4
Fanchin et al [9]	40
Arrayo et al [13]	19.4
Sadek, et al [27]	18
Mahwshwari et al [11]	8.9
Trout , et al [7]	14
Kamel and Ahmed [15]	15
Panayotidis 2000 [14]	16.47

The FSP had not shown superior results for all the indications of insemination in comparison with the IUI. However it is widely considered as more efficient technique and suggested to be appropriate for cases with unexplained infertility. The pregnancy rates of previous authors concerning unexplained infertility are shown in the Table II.

Figure 2

Table 2: FSP pregnancy rate for unexplained infertility, studies of 1992 to 2002

Studies 1992 to 2002	Unexplained infertility
Kahn, et al [1]	26,7
Kahn, et al [4]	27
Kahn, et al [3]	29
LI [5]	24
Karande, et al [12]	11.8
Gregoriou, et al[10]	14,5*
Mamas [30]	30,36
Mamas [8]	26,3
Nuojua-Huttunen et al [16]	8
Trout , et al [7]	16
Panayotidis [14]	31,3*
Ricci , et al [6]	24.2

* non statistical difference comparing IUI

Some of the raisons that could interfere for these results:

1. The statistical power of each research is not clearly indicated in alll published paper. Larger sample is therefore likely to be necessary for the groups, to be more representative of the population. It was impossible to estimate the theoretical number of the couples with each cause of infertility that usualy is presented to the centre beforehand. Homogenisation concerning demographical parameters is esential as well detailed criteria about the diagnosis of infertility (unexplained, female, male or mixte)

2. Another factor that could explain these results is the hypothetical influence of the previous ovarian stimulation treatments in the couple. In the studies with consecutive cycles many authors gave very encouraging results in pregnancy rate for the FSP, of 20% to 40 % (Kahn et al., 1993[3] [4], Li 1993 [5], Fanchin et al., 1995 [9]). In contrast other authors have reported mediocre results for the FSP ie 9% or 14.5%, (Gregoriou et al., 1995 [10], Mahwshwari et al., 1999 [11]). Studies without precisions concerning previous stimulated cycles by technique, gave rates of between 11.8% (Karande et al., 1995 [12]) to 19.4% (Arrayo et al., 1995 [13]) for the FSP technique.Panayotidis 2000 [unpublished data 14]: The results of this study do not show a statistically significant superiority of the FSP over the IUI method in the175 included cycles, (FSP 16.4 versus 12.2 IUI, despite the 4 % difference of the total pregnancy rate between the FSP and IUI.The 4% difference between FSP and IUI in this study is consistent with those of recent studies of Trout and Kemman 1999 [7], Kamel and Ahmed 1999 [15] that report a 4% rate superiority of the FSP versus IUI technique. The work of Nuojua-Huttunen et al., 1997 [16] who studied only the first insemination without regard to the type of infertility, did not show this difference of 4%.

3. Since 1992 different protocols about ovarian stimulation are applied: Clomiphene, alone or combined with FSH, mFSH used. And different cirteria of ovarian induction have been used (diameter of follicule, number of follicules, total number of FSH ampoules administrated, endometrium, and ultrasonographic monitoring).

4. Since 1990 better techniques of sperm preparation are used (density three-layer centrifuged gradient separation, swim-up etc). The quality of the sperm preparation finaly used is in direct dependance of the separation technique.

5. Very important work was the meta-analysis realized by Trout and Kemman 1999 [7], demonstrated a significant difference of superiority for FSP concerning the unexplained hypofertility, 22% versus 13% for IUI. Their work also presented a tendency towards superiority of FSP versus IUI in pregnancy rates on the unexplained hypofertility with 27% for FSP versus 8% IUI. They included all the previous studies (from 1992 to 1998) but exempted Fanchin et al., 1995 [9] [17] who did not detail their indications/ results and Karande et al., 1995 [12] [18].The most important difficulty for a meta-analysis is the inclusion of the population groups under the same definition criteria (diagnosis, complementary exams). Finally they included 5 studies (Kahn et al., 1993 [4], Gregoriou et al., 1995 [10], Mamas 1996 [8], Nuojua-Huttunen et al., 1997 [16], Trout and Kemman 1999 [7]) giving 610 cycles (293 IUI and 317 FSP) demonstrating significant superiority for FSP. All the studies included had in common the technique of FSP but not in the method used (Foley, DNB speculum, Allis pence, ZUI catheter) or in the protocol of ovarian stimulation combined gonadotropins (hMG with /or FSH) with or without CC. Only the patients with unexplained infertility

had a statistically higher pregnancy rate with fallopian sperm perfusion (odds ratio, 4.1; confidence interval, 1.1-16.4). A meta-analysis of the prospective randomized trials that provided data on patients with unexplained infertility showed a significant improvement in pregnancy rates with fallopian sperm perfusion (odds ratio, 1.9; confidence interval, 1.2-3)The definition of unexplained Hypofertility is not always detailed. No evaluation was made concerning the different methods of FSP.

6. Actually we do not know which method of FSP is the most efficient. A meta-analysis with the same method of FSP and under experienced operators could be more powerful.

7. Despite the FSP seamed more efficiant than IUI, few studies were realised Good designed research of comparison with larger populations, 2 to 3 years are necessary. There are few works on this subject since 1992. The last meta-analysis had helped in the scientific reflection and suggested the interest of the FSP in the unexplained infertility.

8. The factor of the operator-doctor was considered constant until now and could possibly influence the results of the FSP. There is no work on this domain, to evaluate this possibility. If the operator is not convinced about the technique (IUI or FSP), would the inseminations be less successful? We do not know if the other studies were done by experienced colleagues, or if the use of the FSP were in the quotidian practice of the medical centre where the study have been held. We do not know if the learning stages of the technique influenced the results; Panayotidis 2000 [14] study, the medical team were mostly first time users oh this FSP technique and some participating doctors had performed only few of these before. Nevertheless all the inseminations were included. Could this heterogeneous application of insemination and operator experience influence the realization of a meta-analysis? Trout and Kemman 1999 [7] advocate that the doctor or the couple having knowledge of the technique used does not influence their results, (no other details in their article).

9. The total number of spermatozoa inseminated, does not seem to influence the efficacy of the FSP. Efforts are nevertheless made to preserve the largest quantity in the volume of the spermatic preparation. In the literature, it seems that the total number of spermatozoa do not play a determining role on the pregnancy results, (Dodson and Haney 1991 [19], Evans et al., 1991 [20]). Some medical teams tried to determine limits (under which either no pregnancy occurs or occurs with much difficulty) but the range was too large, varying from 1 X10 6 spermatozoa /ml to 5 X 10 6 /ml with a minimum of 0.3 X 10 6 /ml, (Paulmyer-Lacroix et al., 1998 [21]). Exemple Panayotidis 2000 study [14], pregnancies were obtained with a minimum of 0.6 X 10 6 /ml for the FSP and 2.88 X 10 6 /ml for the IUI. The mean for the successful cycles was 14.8 X 10 6 /ml spermatozoa inseminated for the FSP and 6.21 X 10 6 /ml for the IUI technique. The unsuccessful cycles had a mean 11.2 X 10 6 /ml for the FSP and paradoxically 8.19 X 10 6 /ml for the IUI.

10. The difference between the FSP and IUI is in the final place of arrival of the spermatozoa. Along the female reproductive tract (woman with normal fallopian tubes), there is a progressive loss of spermatozoa numbers (Mortimer and Templeton, 1982 [22], Keck et al., 1997 [23]). Mortimer, 1983 [24], estimates that 200 spermatozoa would remain into the fallopian tubes and this quantity was stable despite initial inseminated numbers of spermatozoa being increased 100 to 1000 times. The FSP increases the intrauterine pressure, 70-200 mmHg, necessary for a flush influx of spermatozoa directly into the fallopian tubes, (Li 1993 [5], Fanchin et al., 1995 [9], Baker and Adamson, 1995 [25]). This increased pressure may help the spermatozoa to by-pass possible obstacles in the fallopian tubes from membranes to mucus, existent during the peri-ovulatory period, (Amso et al., 1994 [26], Li, 1993 [5], Fanchin et al., 1995 [9], Sadek et al., 1998 [27]). The FSP offers the possibility of achieving a higher spermatozoa concentration in the peritoneal cavity than the IUI. If this is the only reason for better results with FSP, then theoretically better results might be observed for all the infertility sub-groups.

11. It is unknown why the FSP has better results only in the unexplained infertility group compared to other groups. The more accepted hypothesis is the existence of a similar mechanical effect created following a hysterosalpingography, (Li 1993 [5], Fanchin et al., 1995 [9] Trout and Kemman [7], 1999 Sadek et al., 1998 [27]). Very often after hysterosalpingography, higher pregnancy rates are observed in the next cycle. Sometimes the complementary investigations do not determine the presence of micro-obstructions in the tubes. Perhaps the FSP helps to surpass these obstacles.

12. Certain studies do not detail their results by sub-group and give the total pregnancy rate (Fanchin et al., 1995 [9] Karande et all., 1995 [12]). It is obvious that the majority of studies give results for the unexplained infertility group of more up to 20% pregnancy rate. The work of Mamas, 1996 [8] and Kahn et al., 1992 [1], gave a statistical significant rate of more than 26 % for FSP. Some times higher pregnany rates are calculated but not statistical significant because of restricted tested group, Panayotidis 2000 [14]: 31% FSP versus 5.5 % IUI (34 total cycles with unexplained infertility).

13. In the literature the results concerning the IUI for unexplained hypofertility were varied, from 4% (Paulmyer-Lacroix et al., 1998 [21]) to 16.6 % (Panel et al., 1995[28]) and were difficult to evaluate (Abboud et al., 1999 [29]). Most acceptable rates are near 12% for unexplained infertility with IUI.

14. The simplicity of the FSP was mentioned in all comparative studies. Sometimes reflux was observed. This could be prevented with slow perfusion 1 ml/per minute [1]. When the intrauterine catheter is empty of sperm preparation the operator may need to wait for 4-5minutes and then remouve the catheter. Mild reflux does not seem to influence the results of the FSP but in contrast significant reflux (> 0.4 ml) did not result in a pregnancy. Simultaneous ultrasonography may prevent the precocious removal of the catheter [14], may evaluate the quantity of the sperm preparation into the intrauterine cavity and may help in the decision to complete the FSP procedure (i.e. timely removal of the catheter). In the medical centres where the use of ultrasonography is not technically possible, attempt to reaspirate with the intrauterine catheter after the end of the insemination by periods of 5 minutes [8] could be valuable for the operator; if there is no return of the preparation in the catheter then, all of the inseminate preparation is presumed to have passed into the tubes and the intra-peritoneal cavity, This will enable the catheter and the speculum to be withdrawn without (a priori) any reflux.If more than 1 ml comes back in the catheter, the operator need to wait for a few minutes and re-inseminate again.

15. All of the authors agreed that the women tolerated the FSP technique very well. The FSP using the DNB speculum® [8] also presents some advantages in practice and in economical costs. It is easy to perform and there is no inconvenience as described for the FSP using the paediatric Foley's catheter (Mamas 1996 [8], Fanchin et al., 1995 [9]). The Foley's catheter is cheaper but is sometimes very difficult to introduce into the cervical canal. It is important to push the sperm preparation to the extremity of the catheter (also to force away the air space) simultaneously avoiding desterilization of the material. This operation takes time before the FSP procedure can be carried out. The catheterisation is not always easy; the use of a clamp is necessary with risk of spermatic leak. The use of the FAST system® for FSP can be expensive and very few times the placement of the seal cup on the cervix is not perfect. Recently a new application of a FAST variation device appears to be a little more expensive than the classical IUI, (Ricci et al., 2001 [6]). The Allis clamp sometimes results in discomfort to the women and also reduces the operator's view. The hypothesis of interference of the Foley catheter material with the spermatozoa is not elucidated at present, (Nuojua-Huttunen et al., 1997 [16]). Most of the studies used the same catheter for each of the two techniques.

FUTURE USE OF FSP

The FSP has a place for inseminations with donor sperm. Only two studies gave encouraging significant results, (Kahn et al., 1992ß [$_{2}$], Mamas, 1995 [$_{30}$]). These situations (only

for male infertility and normal woman) are equivalent to unexplained hypofertility. If the FSP continues to give better results a research is indispensable on donor insemination. Other interesting domain of FSP application is the immunological infertility with presence of anti-spermatozoa antibodies. This kind of hypofertility is rare and not well elucidated (Almeida, 1998 [31]). The existence of these antibodies does not always correlate with infertility (Almeida, 1998 [31], Gautam et al, 1998 [32]); recent research showed that anti-spermatozoa antibodies also exist in higher parts of the female reproductive tract (Hiroaki et al., 1995 [33], Shibahara and Wilwlm, 1995 [34], Bates, 1997 [35]). The theoretical interest of the FSP is in the increased concentration of spermatozoa in the fallopian tubes and the intra-peritoneal cavity. The use of a washed spermatic preparation with FSP could give rapidly a larger number of spermatozoa and decrease the chances of contact with these antibodies. The IUI might have the disadvantage that the spermatozoa must go up, passing along the uterine cavity and go out from the tubes with many possibilities of contact with these antibodies. The IUI gives mediocre results in this domain of hypofertility, from 5% to 15%, (Ombelet et al., 1997 [36]).

In cases where the immunological factor is not responsible for hypofertility the repeated use of the FSP could possibly induce the production of anti-spermatozoa antibodies with the increased (non physiological) concentration of spermatozoa in the intra-peritoneal cavity, Kahn et al., 1992a [1]. This hypothesis could also explain the diminution of the pregnancy rate after multiple FSP. Only one study searched this eventually, Kahn et al., 1993c [37], with the conclusion of no correlation or increased production of these antibodies with FSP. In a future study it would be interesting to measure the benefit of the mechanical un-blocking effect of the FSP and the theoretical induction of anti-spermatozoa antibodies.

CONLUSION

Fallopian sperm perfusion does not improve the chances of pregnancy in patients with infertility other than those with unexplained infertility. If in a future well designed study the benefits of FSP are confirmed statistically and demonstrate superiority with larger populations, then the FSP could replace the IUI in certain indications for artificial insemination and could be an alternative for couples before embarking on IVF treatment.

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