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Research Article

The Role of Evie in Increasing Success Rate of Intrauterine Insemination

Mohamed Mohamed Khalafalah[1]* and Mohamed Farghali[2]

[1]*Lecturer of Obstetrics and Gynecology, Menofia University, Egypt*

[2]*Assistant Professor of Obstetrics and Gynecology, Ain Shams University, Egypt*

***Corresponding Author:** Mohamed Mohamed Khalafalah, Lecturer of Obstetrics and Gynecology, Menofia University, Egypt.

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Abstract

Purpose: Intrauterine insemination (IUI) is a fertility treatment that involves placing sperm inside a woman's uterus to facilitate fertilization. Slow releasing sperm method is Simple and safe approach. We therefore tested the reliability and efficacy of the use of Evie as a method of IUI.

Methods: This study was carried out at a private polyclinic center in Kuwait between March 2013 and June 2014. The study included 100 patients divided in 2 groups: first group was treated by ordinary IUI and second group was treated by Evie IUI. The end-point of the treatment cycle was either a negative pregnancy test or a positive test confirmed by clinical evidence of pregnancy in the form of intrauterine gestational sac visualized by ultrasound 2 weeks after positive biochemical test.

Results: A total of 100 patients with primary or secondary infertility either due to male factor, anovulation and unexplained infertility were treated by IUI, 50 patients were treated by conventional IUI, the other 50 patients were treated by Evie method. Total 17 patients got pregnant as diagnosed by positive pregnancy test after 14 days of insemination. 10 patients achieved pregnancy who were in Evie group whereas, 7 patients conceived in ordinary IUI group.

Conclusion: Slow releasing sperm method of IUI is a good and effective method. It has a high success rate in comparison too conventional IUI.

Keywords: *Intrauterine insemination; fertilization; woman's uterus; sperm; clomiphene citrate*

Introduction

Intrauterine insemination (IUI) is a fertility treatment that involves placing sperm inside a woman's uterus to facilitate fertilization. The goal of IUI is to increase the number of sperm that reach the fallopian tubes and subsequently increase the chance of fertilization. IUI provides the sperm an advantage by giving it a head start, but still requires a sperm to reach and fertilize the egg on its own [1].

Before intrauterine insemination, ovulation stimulating medications may be used, in which case careful monitoring will be necessary to determine when the eggs are mature. The IUI procedure is then performed around the time of ovulation, typically about 24 - 36 hours after the surge in LH hormone that indicates ovulation will occur soon [2].

A semen sample washed by the laboratory to separate the semen from the seminal fluid. Following which a catheter used to insert the sperm directly into the uterus. This process maximizes the number of sperm cells that are placed in the uterus, thus increasing the possibility of conception. The IUI procedure takes only a few minutes and involves minimal discomfort [3].

The success of IUI depends on several factors. If a couple has the IUI procedure performed each month, success rates may reach as high as 20% per cycle depending on variables such as female age, the reason for infertility, and whether fertility drugs were used, among other variables. While IUI is a less invasive and less expensive option, pregnancy rates from IUI are lower than those from IVF [4].

A new method for intrauterine insemination (IUI) uses slow introduction techniques for the prepared sperm using an EVIE pump. This is a device that allows prepared sperm to be injected into the uterus slower than it occurs under the use of the traditional IUI method [1].

The EVIE device comprises of a catheter which is introduced into the uterus, the pump with a chronometer, an insemination syringe and a strap. Using the strap, the device is fastened to the woman`s thigh. The pump then slowly injects prepared sperm into the uterus. During this process the woman can lead a normal way of life, removing the device several hours later. This patented device was presented at the conference of the European Society of Human Reproduction and Embryology (ESHRE) in Rome in 2010 and aroused a big interest. The EVIE product was tested both in Europe (CE marking), and in USA (FDA). It has been used in clinical practice since 2011 [6].

The pump enables sperm to be released slowly into the womb over a three to four-hour period. By mimicking the natural process, this slow release system enables the 'window of opportunity' to be longer, giving more sperm more time to reach the egg. It also prevents the loss of sperm that can happen in conventional IUI treatment [7].

With most traditional IUI treatments, all the sperm are released into the womb at once, flooding the egg with too many sperm. When this happens, the egg is overwhelmed and often becomes unable to accept any sperm at all and so the fertilization attempt fails. With this system, the egg is more receptive to being fertilized by the sperm and the success rate is similar to the more invasive IVF treatment [8].

IUI is indicated in many diagnostic conditions. Male infertility is the most common indication. IUI is indicated for all categories of unexplained infertility and for couples with minimal and mild endometriosis. Patients, awaiting IVF or who cannot afford IVF, may try IUI at first [9].

Aim of the study

The aim of the study is to evaluate the effect of Evie in increasing the success rate of IUI.

Patients and methods

This study was carried out at a private polyclinic center in Kuwait between March 2013 and June 2014. The indications of IUI: male factor, anovulation and unexplained infertility. The study therefore included 2 groups: first group was treated by ordinary IUI and second group was treated by Evie IUI. WHO standards (WHO Laboratory Manual, 1999) for sperm concentration for motility, and with Kruger's strict criteria for sperm morphology were applied to differentiate between fertile and sub fertile criteria. Semen samples were evaluated at an interval of at least 3 months the semen analysis. For male factor group, the inclusion criteria were motile sperm with counts > 1 × 106/ml in the fresh specimen and a normal sperm morphology of ≥ 5% along with a normal female partner, whereas, patients with ejaculatory dysfunction and, semen parameters below the above-mentioned lower cut-off values were excluded from the study.

The unexplained infertility group had normal findings in seminal fluid analysis, mid-luteal serum progesterone and hysterosalpingogram or laparoscopy. The study included 100 patients who were given clomiphene citrate (CC) for ovulation induction with or without Human Menopausal Gonadotropins (hMG). Induction of ovulation started by Oral tablets of CC (50 mg) in doses of 100 mg/day from the third to seventh day of the cycle, was followed by hMG sequentially from the eighth day. The hMG dose was titrated against ovarian response to obtain one to four follicles of 18 – 20 mm mean diameter as shown by serial transvaginal sonographic (TVS) monitoring started on the 10th day of the cycle and repeated every other day until the day of ovulation triggering. Once the mean diameter of the leading follicle reached ≥ 18 mm, the hCG dose (10000 IU) was given. Cycles were cancelled when large follicles (mean diameter ≥ 16 mm) were

more than four in number (to avoid multiple pregnancies) and/or when medium-sized follicles (mean diameter 12 – 15) were ≥ 10 in number (to avoid hyperstimulation syndrome).

At the time of insemination, the occurrence of ovulation was checked first by transvaginal ultrasound Following which an insemination procedure was scheduled for 34-38h after hCG injection (i.e. 36 ± 2 h). Once ovulation was diagnosed (evidence of follicular rupture as shown by the presence of free fluid in Douglas pouch and visible corpus luteum and/or disappearance of follicles), insemination was done. Luteal phase support in the form of progesterone 100 mg vaginal tablets was prescribed twice daily.

A pregnancy test (serum β-hCG level) was scheduled 14 days later. The end-point of the treatment cycle was either a negative pregnancy test or a positive test confirmed by clinical evidence of pregnancy in the form of intrauterine gestational sac visualized by ultrasound 2 weeks after positive biochemical test. The study was approved by the ethical committee and all patients informally consented for the procedure. To obtain seminal sample, patient s husband was instructed to abstain from sexual intercourse for 3 days before insemination following which then semen sample was collected through masturbation in a sterile plastic container. If semen found normal after liquefaction, then it was processed using the swim-up method. In case of abnormal semen parameters other than exclusion criteria, mini swim-up method was used.

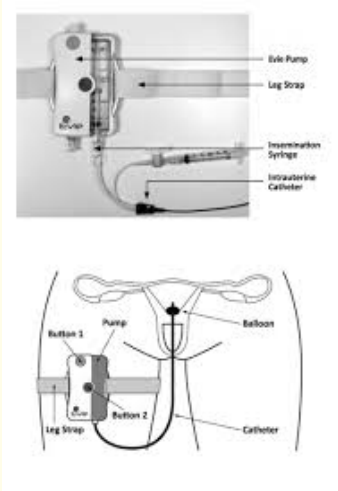
In the swim-up method, 1 ml of insemination media is mixed with an equal volume (1: 1) of semen, while in the mini swim-up method, the ratio is 1: 3. The suspension is then centrifuged for 10 min at 300g, or 3-5 min at 500g. The mixture is kept for about 45 min at 37°C. Then the upper top 0.6 ml is separated in a test tube and insemination is carried out using Evie.

Evie involves delivering approximately 1 ml sperm into the uterus over a 3-4 hour period. Each Evie kit comprises:

1. Evie Pump (Disposable, single use), devised for slow-release insemination of sperm.
2. Intrauterine Sterile Catheter (Disposable, single use) (Length 28cm, Diameter (OD): 5 Fr, maximum balloon inflation: 1ml, devised to deliver sperm to the uterus
3. Sterile Insemination syringe (Disposable, single use) (Volume: 3ml), to contain and deliver sperm to the catheter.
4. Leg strap (non-sterile).

Evie was not used if physical damage had occurred but this did not happen in our study.

Precautions were done to protect Evie from damage like: During transportation: the sterile packaging of the catheter and the syringe were intact, expiration date has not passed, the syringe and catheter were supplied within the kit is used and catheter balloon was inflated gradually using sterile saline. The catheter was gently inserted into the uterus through the cervical canal, similar to a standard IUI or HS procedure.



The steps of procedure

Before starting the procedure: The patient lied in the lithotomy position with a speculum inserted. The vagina and cervix were cleaned using normal saline solution. Uterus was sounded to determine uterine depth.

Procedure: Leg strap was attached to pump and pump was subsequently attached to patient's right leg. pump was oriented with Button 1 toward patient's head. I The supplied insemination syringe was filled with 1.5 ml of prepared sperm. Catheter was removed from sterile package with attached balloon inflation syringe yellow tip protector was discarded. insemination syringe was connected to catheter injection line. catheter was flushed by advancing insemination syringe to1.0 ml. Insemination syringe should not be disconnected at this time inflation syringe was disconnected from balloon inflation line of catheter and syringe was filled with no more than 1 ml sterile saline. Balloon inflation syringe was re-connected to open stopcock. Catheter was inserted into the uterus to sounded depth using depth marks as a guide.

Gradual inflation of balloon was performed with 1.0 ml saline was happened. followed by the stopcock to maintain balloon inflation. Next step involved pulling back gently on the Catheter shaft was pulled back to seat balloon against and seal internal cervical os.

Pump cover was removed by pressing release tab at top of pump next to button 1. Insemination syringe was inserted into cradle of pump. Syringe wings and plunger end must lie between tabs and syringe lever arm to ensure proper operation of syringe.

With syringe in place, cover on pump is re-installed by first inserting tab at bottom of pump before finally locking tab at top of pump. Balloon inflation syringe was disconnected and discarded. Pump was activated by pulling out red safety tab and firmly pressing Button Starting Time was recorded.

Instructions for Removal

We explained the following instructions to the patient for removal of this device:

1. Patient was asked to firmly push the Button 2 until it moved inward, after 4 hours. Patient should make sure that the button remains depressed a few seconds, or she should depress it several times to ensure that all sperm has been delivered.

2. She should open stopcock on catheter to deflate balloon, as withdrawing the catheter with an inflated balloon may cause pain. A small quantity of saline may be expelled after balloon is inflated.

3. Catheter should be withdrawn gently and the leg strap should be released.

4. The entire device should be placed in the disposal bag supplied and should be discarded appropriately.

Results

The study was carried out during one year and 3 months on 100 patients. Total 17 patients got pregnant as diagnosed by positive pregnancy test after 14 days of insemination. 10 patients achieved pregnancy who were in Evie group whereas, 7 patients conceived in ordinary IUI group. The age of the patients ranged between 22 to 39 (mean age: 29 years). 84% of the patients complained of primary infertility and 16% were suffering from secondary infertility. The duration of infertility was between 2 and 6 years. Out of total 17 patients who conceived, 9 patients had secondary infertility and 8 with primary infertility.

The results showed that anovulation was the cause of infertility in 51% of patients while unexplained infertility in 45% of patients and male factor in 4% of them.

	Ordinary IUI (*n =50*)	**IUI with Evie (*n = 50*)**	***p***
Age (years)	28.5 ± 4.9	29 ± 4.0	0.3
BMI (kg/m^2)	24 ± 2.1	23.8 ± 2.9	0.47
Duration of infertility (years)	3.8 ± 2.1	4 ± 2	0.34
Type of infertility			
Primary	41(82%)	43(86%)	0.45
Secondary	9 (18%)	7(14%)	0.45
Indication of IUI			
Unexplained infertility	22(44 %)	23(46%)	0.66
Anovulation	26 (52%)	25(50%)	0.59
Male factor	2 (4%)	2(2%)	1.0

Table 1: *Demographic data of both studied groups.*

Table 2 showed that there is no difference between patients treated with conventional IUI and Evie as regarding days of stimulation, total number of follicles (LD0) and mean follicle diameter (LD0) (mm)

	Ordinary IUI (*n = 50*)	**IUI with Evie (*n = 50*)**	***P* Value**
Days of stimulation	11.1 ± 2.05	11 ± 2.03	0.63
Total number of follicles (LD0)	2.36 ± 1.2	2.3 ± 1.05	0.61
Mean follicle diameter (LD0) (mm)	19.4 ± 2.5	19.8 ± 2	0.4

Table 2: *Stimulation characteristics of both studied groups.*

LD = Luteal day.

Table 3 showed significant difference between difference between patients treated with conventional IUI and Evie as regarding the level of LH after triggering.

	Ordinary IUI (*n = 50*)	IUI with Evie (*n = 50*)	*P* Value
Basal LH level (mIU/ml)	3.95 ± 1.5	4.1 ± 1.4	0.33
LH level 12 h after triggering (mIU/ml)	75.9 ± 8.8	13.5 ± 4.9	< 0.001
Progesterone level before triggering (ng/ml)	1.1 ± 0.5	1.01 ± 0.61	0.09
LD 8 progesterone level (ng/ml)	40.0 ± 7.1	38.9 ± 7.0	0.14

Table 3: *Circulating level variation of both LH and progesterone among both groups.*

Table 4 showed that 6 patients treated with conventional IUI got pregnancy whilt 9 patients treated with Evie got pregnancy.

	Ordinary IUI (*n = 50*)	IUI with Evie (*n = 50*)	*p* Value
Luteal phase length (days)	13 ± 1.03	12.9 ± 1.04	0.34
Biochemical pregnancy (cycle)	7/50 (14%)	10/50 (20%)	0.2
Clinical pregnancy/(cycle)	6/50 (12%)	9/50 (18%)	0.23

Table 4: *Luteal phase length and pregnancy rate in both groups.*

Discussion

The Evie increases the window of opportunity for conception, and significantly enhances the success rate of IUI at little extra cost. This may allow a couple to avoid more expensive and invasive techniques such as IVF, and is simple and fairly user-friendly. There is no sperm leakage such as is typically experienced during conventional IUI and the Evie has nearly a 10% higher rate of success than typical IUI. Similar studies have been conducted in England, Germany and Israel [8].

According to the results of those studies up to 30% of patients treated using the EVIE device were successfully fertilized. This value is very close to the success rate when using the IVF method. The application of the EVIE method can help to improve the treatment results [8].

Advantages of Evie are very close approximation of the natural procedure in which the spermatozoa arrive to the fertilization site over a long period. An extended "window of opportunities" for meeting between the ovum and spermatozoa will be longer [9].

There is no loss of spermatozoa due to leaking as sometimes happens with single-time injection practiced in the IUI method. Proper selection of patient for intrauterine insemination may increase the rate of success. Although Evie being simple but still an expensive way to increase the success rate of IUI, we do recommend that Evie should be tried after failure of conventional IUI and before referring of the patient to IVF [5].

The study showed no effect of age, body mass index or duration of infertility between patient treated with Evie or conventional IUI. Pregnancy detected by serum pregnancy test and by intrauterine gestational sac was achieved in 9 cases of patients treated with Evie while 6 patients treated with conventional IUI got pregnant so Evie raised the number of patients got pregnancy due to slow releasing of sperms over a considerable time. The study did not search for the causes of failure of pregnancy in cases treated by IUI as the aim of the study is to detect the value of Evie in elevation of success rate of IUI.

Conclusion

Slow releasing sperm method of IUI is a good and effective method. It has a high success rate in comparison to conventional IUI but Evie is also expensive and not easily available method for IUI.

Bibliography

1. Sutter PD., *et al.* "Comparison of Outcome of Pregnancy after Intra-Uterine Insemination (IUI) and IVF". *Human Reproduction* 20.6 (2005): 1642-1646.

2. Thomson F., *et al*. "Obstetric Outcome in Women with Subfertility". *British Journal of Obstetrics and Gynecology* 112 (2005).

3. Allen VM and Wilson RD. "Pregnancy Outcomes After Assisted Reproductive Technology". *Journal of Obstetrics and Gynecology Canada* 28.3 (2006): 220-233.

4. Soria M., *et al*. "Pregnancy Predictors after Intrauterine Insemination: Analysis of 3012 Cycles in 1201 Couples" (2012).

5. J Gomez R., *et al*. "The Effect of Ovarian Stimulation on the Outcome of Intrauterine Insemination". *Archives of Gynecology and Obstetrics* 289 (2014): 181-185.

6. Ahinko-Hakama., *et al*. "Success in Intrauterine Insemination: The Role of Etiology". *Acta Obstetricia et Gynecologica Scandinavica* 86 (2007): 855-860.

7. The ESHRE Capri Workshop Group "Intrauterine Insemination". *Human Reproductive Update* 15 (2009): 265-277.

8. Gomez, R., *et al*. "The Effect of Ovarian Stimulation on the Outcome of Intrauterine Insemination". *Archives of Gynecology and Obstetrics* 289 (2014): 181-185.

9. Reindollar RH., et al. "A randomized clinical trial to evaluate optimal treatment for unexplained infertility: the fast track and standard treatment (FASTT) trial". *Fertility and Sterility* 94.3 (2010): 888-899.

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