Summary

When the results of a standard infertility evaluation are normal, practitioners assign a diagnosis of unexplained infertility. Although estimates vary, the likelihood that all such test results for an infertile couple are normal (i.e., that the couple has unexplained infertility) is approximately 15% to 30% ***(The practice committee of the ASRM, 2006).***

If a completed investigation for infertility has not revealed any cause of infertility , clomiphene citrate and insemination is often tried as the first- line treatment ***(Verhulst et al., 2006)*** or in combination with gonadotropins or gonadotropins alone ***(Hughes et al., 2001)*** . IVF is usually offered as a second treatment option, but the most effective way of obtaining pregnancy for couples with unexplained infertility has not yet been clearly demonstrated ***(Pandian et al ., 2005).***

Insemination can be carried out while the couple is on the waiting list for IVF. Clomiphene citrate and insemination has an average pregnancy rate of 8% per treatment cycle ***(Guzick et al., 1998).*** With an increasing number of infertile years, the pregnancy rate per treatment cycle will be gradually reduced due to attenuation bias ***(Hull,1992).*** The success rate with clomiphene citrate and insemination cycles is thus substantially lower than the overall approximately 35% pregnancy rate per IVF cycle.

Pregnancy rates have been recorded after HSG or after sonohysterography. Tubal flushing with lipiodol has been tried in a small, randomized clinical study on women with endometriosis and no spontaneous pregnancy for 3 years ***(Nugent et al., 2002).***

After perturbation with lipiodol, 30% of the patients achieved pregnancy compared with none of the patients randomized to expectancy. However, there are occasional reports of serious complications after HSG using oil – based contrast, presumably due to fat embolism ***(Uzun et al., 2004).***

Compared with an oil – based contrast medium which can remain intraperitoneally ***(Miyamoto et al., 1995),*** a local anaesthetic such as lignocaine is a well – tolerated drug and has the same capacity in vitro to reduce sperm phagocytosis ***(Edelstam et al., 1998).*** Perturbation with lignocaine (0.1 mg/ ml) in a balanced salt solution was tried in a previous clinical study with the same overall pregnancy rate as was described with. Lipiodol ***(Edelstam et al., 2001).*** No complications were noted with low – dose lignocaine perturbations and no reproductive toxicological problems have been described ***(Ramazzotto et al., 1985).***

The effect of adding tubal flushing/perturbation during an insemination cycle is presumed to have two effects: mechanical and immunological. The mechanical effect is thought to be the opening of loose adlhesions around the fimbriae ***(Rasmussen et al., 1991).*** The in vitro observed reduced sperm phagogytosis is presumed also to have an immunological effect in vivo by enhancing the survival rate of spermatozoa ***(Edelstam et al., 1998, Nugent et al., 2002).***

This was a prospective randomized controlled study conducted in assisted reproduction unit in Benha University Hospital & Private Fertility Center from December 2009 till September 2011.

The study included 115 couples having at least 1 year of unexplained infertility or clomiphene citrate failure (achieving ovulation but failure to achieve conception

after 6 months of taking clomiphene citrate). Complete evaluation was done by history, examination and investigations.

The couples were randomized into 2 groups:

Group 1 (odd numbers):

Couples received 100 mg clomiphene citrate /daily from day 3-7 of the menstrual cycle. Monitoring was done by vaginal ultrasound till the leading follicle was ≥ 18 mm in diameter. Then 5,000 IU of hCG was given to the patient and intrauterine insemination was done 24-36 hours later.

Group 2 (even numbers):

Couples received 100 mg clomiphene citrate /daily from day 3-7 of the menstrual cycle. Monitoring was done by vaginal ultrasound till the leading follicle was ≥ 18 mm in diameter. Pertubation was done using Lidocaine. Then 5,000 IU of hCG was given to the patient and intrauterine insemination was done 24-36 hours later.

One hundred and fifteen couples were enrolled in this study. Sixty cases in group 1(IUI only) and fifty five in group 2 (lidocaine+IUI). The demographic variation in the clinical data, type of infertility, hormonal variation and ultrasonic criteria were evaluated between both groups, between pregnant and non-pregnant cases and finally between pregnant cases in both groups.

There were no significant differences in the clinical data, type of infertility, hormonal variation and ultrasonic criteria between both groups. But pregnancy rate was higher in group 2 (14.5% n=8) than group 1 (10% n=6).

The advantages of this work were the induction of ovulation by clomiphene citrate was accepted by the patient as it's commonly used, cheap, oral (no injections), rare side effects, very rare complications.

Tubal flushing with lidocaine so washing out any mucous plugs, or fimbrial adhesion and even may be beneficial in undiagnosed cases of endometriosis, no side effects or complications were reported except for some abdominal discomfort during tubal flushing in 20% of the cases, no complications were reported for lidocaine use, it's an easy to learn procedure that anyone can do it& cheap.

IUI was done the following day which was accepted by all the patients, an easy, minimally invasive cheap procedure; in addition IUI gives the opportunity to examine the semen sample by ourselves and discovering the fallacies in the semen analysis in some couples.

As for the results, although the difference in pregnancy rate between both groups in the study didn't reach a statistically significant difference but there were a higher pregnancy rate in group 2 (IUI+lidocaine). Also the ongoing pregnancy rate and live birth rate were both very promising.

On the other hand, only two disadvantages, the first is that the patient had to come 2 times for the tubal flushing with lidocaine then for IUI in group 2 (lidocaine + IUI) but on the other hand, group 1 (IUI only) attended only once for IUI. The second one was the lower pregnancy rate (14.5%).

But this pregnancy rate although low is an accepted and may be even relatively high compared to other approaches irrespective of IVF&ICSI. Of course, IVF has the highest pregnancy rate and may be the shortest and fastest way to achieve pregnancy but it's also the most expensive line of treatment and it's not covered in the health insurance of most of the population.

So, the approach of ovulation induction with clomiphene citrate, tubal flushing with lidocaine and finally IUI, a reasonable and a cheap line of treatment for cases of unexplained infertility in low income communities.

In conclusion, it's an option that should be evaluated in a large randomized trial and especially in cases with previous IUI failure as there is an increase in the pregnancy rate. This increase in pregnancy rates range between 30-40% should be explained to the partners. The procedure is simple, safe, and cheap which makes it worth trying, impregnating 12-14% of the cases, before landing on IVF.