

Original Research Article

PROSPECTIVE CROSS-SECTIONAL STUDY OF INTRAUTERINE INSEMINATION WITH HYDROTUBATION IN WOMEN WITH INFERTILITY

Abstract:

Background: Hydrotubation is the instillation of a solution of medicine through the cervix into the uterus and fallopian tubes under pressure into the peritoneal cavity. It has little value to test whether or not the tubes are blocked in the investigation of infertility and therapeutically to flush or clean the fallopian tubes.

Methods: Sixty women with unexplained infertility were scheduled randomly for hydrotubation either with saline or low dose Lidocaine in saline. Hydrotubation was carried out one day before intrauterine insemination in clomiphene citrate stimulated cycle. Outcome measures were rates of pregnancy, first trimester abortion, ectopic pregnancy, multiple pregnancy and procedure related pain.

Results: There were higher clinical pregnancy rates in Lidocaine group which had when compared with saline group but statistically no significant difference found.

Conclusion: Hydrotubation with low dose Lidocaine in saline one day before IUI allowed a significant higher pregnancy rate when compared to saline alone in couples with unexplained infertility.

Keywords: Infertility, Hydrotubation, Lidocaine, Saline, HSG.

Comment [S1]: You must mention (antibiotics, steroids) in addition to lidocaine here

Comment [S2]: I think that this is not an outcome

Comment [S3]: The conclusion indicates a significant higher pregnancy rate while the statistical analysis shows non-significant difference between 2 groups

Introduction:

Infertility is "a disease of the reproductive system defined by the failure to achieve a clinical pregnancy

after 12 months or more of regular unprotected sexual intercourse.”⁽¹⁾ The World Health Organization (WHO) estimates that 60 to 80 million couples worldwide currently suffer from infertility.⁽²⁾

Infertility may be classified as primary or secondary. The prevalence of infertility ranges from 7–26% of couples in the reproductive age in the developed countries.⁽³⁾ A number of options of assisted reproductive technology have since emerged. For patients with unexplained infertility, Controlled ovarian stimulation (COS) with homologous intrauterine insemination (IUI) or in vitro fertilization (IVF) have been found as some of the treatment options available.⁽⁴⁾ The point of intrauterine insemination (IUI) is based on the principle of “increasing the number of gametes (sperms and oocytes) at the right place at the right time.” It helps to bypass the possible cervical factor in couples with abnormal mucus secretions. Intrauterine insemination is a relatively noninvasive and cost effective first-line therapy for selected infertile patients such as having cervical factor, moderate male factor, unexplained infertility, endometriosis, immunological infertility, and infertility due to ejaculatory disorders. IUI in stimulated cycles can be offered in couples with unexplained infertility while waiting for IVF or when IVF is not affordable. Success rate of controlled ovarian stimulation (COS) with intrauterine insemination (IUI) varies between 8 and 22% ⁽⁵⁾

The effect of IUI alone per cycle is small and only of marginal significance. As a result, several advances in the type of stimulation protocols, gonadotropins, tubal flushing, sperm preparation techniques, and ultrasound monitoring have led to promising success rates with IUI.

Tubal flushing or hydrotubation has previously proved to be one way of increasing the chance of achieving conception for couples with unexplained infertility and at early stages of endometriosis. The effect of hydrotubation on fertility can be mechanical and immunological, e.g., inhibition of phagocytosis of spermatozoa and affecting levels of peritoneal factors such as cytokines, also by mechanically flushing out small mucus plugs or releasing flimsy adhesions due to pressure created inside tubes during hydrotubation.⁽⁶⁾ This cross-sectional study was planned to investigate the therapeutic outcome of hydrotubation using antibiotics, steroids, xylocaine and intrauterine insemination in stimulated cycles in women with infertility.

Comment [S4]: It is better to add type of the study (prospective)

Comment [S5]: It is preferred to replace xylocaine by lidocaine as represented in the abstract

Materials and Methods

This study was carried out in patients who came to Wardha Test tube baby center, AVBRH, Wardha. It was a prospective randomized, blinded control trial undertaken between January 2010-March 2011. Patients who fulfilled the inclusion criteria –infertility due to all causes except tubal factor with at least one tube patent were included, both ovaries intact, age less than 40 years were included in this study. The exclusion criteria decided was endocrine disorders like hypothyroidism, pcod, ovarian surgeries, adhesions etc, women with abnormal uterine bleeding, tubal factor infertility. The study protocol was made after taking approval from the INSTITUTIONAL ETHICAL COMMITTEE and written informed consent was obtained. All patients were investigated for bacterial vaginosis, Chlamydia trachomatis and Neisseria gonorrhoeae and infected cases were treated medically before hydrotubation.

The 60 participants were divided randomly into two groups. Randomization will be done according to a computer generated random numerical table.

Ovarian stimulation was done with Tab.Clomiphene citrate 50 mg IBD for 5 days starting from day 2 of the cycle. Starting from day 9 of the cycle, serial folliculometry was done. Endometrial thickness was measured on the day of HCG administration at the greatest diameter perpendicular to the midsagittal plane in the fundal region using transvaginal ultrasound scan using Logiq C5 Machine.

Human chorionic gonadotropin (10,000 IU) was administered intramuscularly as a trigger for ovulation when there will be at least one follicle measuring ≥ 18 mm in mean diameter. Cycle was cancelled if there were 3 follicles ≥ 16 mm in mean diameter or inadequate ovarian response. Hydrotubation was done one day before IUI. Patient will be placed in the lithotomy position with an empty bladder, cervix exposed by a Cusco speculum and parts cleaned.

A Leech Wilkinson's Cannula was inserted into the cervical canal after checking it's patency with normal saline solution, the catheter balloon was inflated with 0.5–1 cc saline and the catheter pulled against cervix. Hydrotubation was done by mixing 20 ml Normal Saline, Inj. Metrogyl 20cc Inj. Dexamethasone 12mg with Xylocaine 1% 2ml in one group and plain Normal saline of equal volume in

Comment [S6]: The study was done 11 years ago??

Comment [S7]: were

Comment [S8]: It is better to mention as polycystic ovarian disease

Comment [S9]: Plz determine type or site of adhesion

Comment [S10]: Or

Comment [S11]: Written informed consents were obtained from cases under the study

Comment [S12]: It is better to mention what IBD stand for

another group. Hydrotubation was performed slowly and steadily. The patients were asked to take rest for 10 min and instructed to come back on the next day for IUI.

Intrauterine insemination was performed 24–36 hrs after administration of hCG, using an intrauterine catheter attached to a 2 ml syringe. Semen was collected by masturbation into a sterile bottle after 2–4 days of sexual abstinence. The standard swim-up technique was used for semen preparation. The cervix exposed and cleaned by using the same technique described during hydrotubation. The cannula was inserted gently into the uterine cavity without touching the fundus and the sperm suspension (0.5–1 ml) gradually released. The patient was advised to take rest in the same position for 15–20 min before discharge. Two weeks after IUI, serum β subunit hCG was measured for identification of pregnancy, confirmed clinically at 6 weeks using ultrasound scan. Only one completed treatment cycle was offered to each couple.

Comment [S13]: It is preferred to give a hint about swim up technique and add a reference for the methodology

Comment [S14]: It is better to mention the system used for HCG measurement

STATISTICAL ANALYSIS

Data obtained were statistically analyzed using the Statistical Package for Social Sciences (SPSS, Chicago, USA) software version 15.0 for Windows. Results were expressed as mean \pm SD, numbers and percentages. Means were compared using the unpaired student's t test while proportions were compared using the chi-square test. Differences were considered of statistical significance if p-value was <0.05 .

Results.

Amongst 60 patients, the mean age group taken were 26 years \pm 2 years in saline group and 27 years \pm 1.8 yrs in lidocaine group. Mean BMI in saline group found was 24.09 ± 1.8 and in lidocaine group it was 25.12 ± 2.1 .

Comment [S15]: Saline hydrotubation group

Comment [S16]: lidocaine hydrotubation group

Out of 60 patients 30 were taken for saline instillation while 30 were given lidocaine. In saline group, 23 patients were found primary infertile cases and 18 primary infertile patients seen in lidocaine group. Mean duration of infertile years seen in both groups were 4 ± 1.2 and 5 ± 1.8 years respectively, as shown in table 1.

Table 1

Patients' demographic characteristics

Demographic characteristics	Saline group (n=30)	Lidocaine group(n=30)	p value
Age	26 ±2.3	27 ±1.8	0.266
BMI	24.09 ±1.8	25.12 ±2.1	0.304
Primary infertility	23 (76%)	18(60%)	0.507
Secondary infertility	7 (23.3%)	12(40%)	0.451
Duration of infertile years	4 ±1.2	5 ±1.8	0.99

Comment [S17]: (years)

Comment [S18]: *

Comment [S19]: *

Comment [S20]: Duration of infertility (years)*

Comment [S21]: (years)

Table 1 describes demographic characteristics in between saline group and lidocaine group in terms of age in saline group varying 26 to 28 yrs and in lidocaine group varying about 27 to 28 yrs. BMI ranging from 24 to 25 in both groups respectively. Primary infertility in saline group were 23 cases while in lidocaine group were 18 cases, however cases of secondary infertility were 7 and 12 in each group.

Table 2 distribution of pregnancy outcomes

	Saline group	Lidocaine group	p value
Biochemical pregnancy	7 (23%)	9 (30%)	0.541
Gestational sac seen	5 (16%)	6 (20%)	0.417
Abortion/preterm / fetal demise	2 (6%)	1 (3%)	0.368
Take home	3 (10%)	5 (16.6%)	0.99

Table 2 shows higher pregnancy rate in lidocaine group as compared to saline group. No cases of ectopic pregnancy were seen in either of the group.

Comment [S23]: Plz mention the fate of the remaining patients (13 out of 30 in saline group and 9 in the lidocaine group)

Discussion

Unexplained infertility is a diagnosis of exclusion. Ovarian stimulation combined with Intra uterine insemination (IUI) is a recommended form of treatment for women with unexplained infertility. Pregnancy rates vary between 10% and 20%, depending upon various factors.(7) Tubal flushing/hydrotubation/pertubation may increase chances of conception in infertile couples by mechanically breaking the flimsy adhesions or decreasing the sperm phagocytosis.(8)

In this study two groups of infertile patients were taken. One group underwent hydrotubation by saline and other were given lidocaine randomly. Retrospectively these patients were studied for their underlying cause of infertility. The success of hydrotubation in different studies carried out in different geographical locations greatly varies.

Comment [S24]: You don not mention the other additives

Aboulghar et al, in their prospective randomized trial of hydrotubation versus no hydrotubation before intrauterine insemination, found results that are not statistically significant yet the conception rate is more

in hydrotubation group.(9) This difference in results could likely be due to difference in demographic features of the study population, the media used for flushing and skills of the surgeon. The better prognosis of this study could be due to carefully selected population with majority of women in younger age group.

Comment [S25]: Your results show no significant difference also like Dr Abulghar et al., study. So no difference between your results and their results.

Today, thanks to ART, tubal disease and tubal factor infertility may easily be overcome. However, many retrospective studies have shown that the hydrosalpinx is associated with poor IVF outcome. The hydrosalpinx fluid possibly acts on two different targets; directly on the transferred embryos or on the endometrium and its receptivity for implantation, or both. There are many theories postulated, but none actually proven(10,11). The results of prospective randomized studies on salpingectomy in women with hydrosalpinges are now forthcoming and have resulted in the Cochrane library recommendation of salpingectomy for hydrosalpinges.(12). The endometrial environment becomes more ideal for implantation with cleaning of embryotoxic cytokines. In a similar way, during the perturbation, thin adhesions in the endometrial cavity was opened with rapid fluid pressure.

Comment [S26]: were

Although the pregnancy rate was higher in the control group, this was not statistically significant when compared with the study group ($p=0.296$). When we evaluated both biochemical and clinical pregnancies, the pregnancy rate was 17.8% in the study group and 23.8% in the control group. The rate of live births, which was the main purpose of this treatment was 12.7% in the study group and 19.8% in the control group.

Comment [S27]: If these are your results, it is better to mention it in the table

Around 10-15% of natural pregnancies end up in spontaneous abortions. Many infertility centers have reportedly shown a much higher incidence in the range of 18–30%, of spontaneous abortion among assisted reproductive technology pregnancies(13). If serial HCG is measured to detect early subclinical pregnancy loss, this rate would increase. In our study, 21% of total pregnancies aborted. This rate was not higher than the expected pregnancy loss rates in normal cycles. When we compared pregnancy loss rates in both groups, there was no significant difference observed ($p>0.05$).

Aboulghar et al. studied 213 patients in a study where, they performed hydrotubation on 103 patients. They used clomiphene citrate and urinary HMG for ovulation induction followed by IUI. In our study, we only used gonadotropins for ovulation induction. Both studies have performed intrauterine insemination after ovulation induction. Aboulghar et al. reported an ongoing pregnancy rate of 12.6% in their hydrotubation group. Similarly, our research resulted an ongoing pregnancy rate of 12.7% in the study group. Therefore our results were compatible with the aforementioned study.(9)

In our study, the control group's fecundability rate was 23.8% and the continued pregnancy rate was 19.8%. There was no significant difference between the study and control groups. However the relatively higher rate in the control group suggested the negative effects of perturbation.

In a prospective randomized study by Edelstam et al. to evaluate the effect of perturbation on pregnancy rates in couples with unexplained infertility, Perturbation was performed prior to ovulation. A total of 130 cycles were investigated. There was a significant difference between the pregnancy rates (14.9 vs. 3.2%) of both groups. The authors concluded that perturbation could be used in conjunction with ovulation induction and intrauterine insemination as a first line management protocol in couples with unexplained infertility.(6)

In a prospective non randomized observational study by Adesiyun et al the authors concluded that with good case selection, therapeutic hydrotubation may be beneficial in resource poor countries, especially in patients with incomplete tubal block (bilateral peritubal adhesions) and as part of treatment for unexplained infertility.(14)

Lei et al. have reported the effects hydrotubation in 50 formerly proven tubal occlusive patients. The hysteroscopic procedure involved the passage of a thin plastic cannula through the fallopian tube

simultaneously using irrigation media that contained hydrocortisone, gentamycin and procaine. The use of additional therapeutic agents in hydrotubation might explain their increased rate of fecundability.

The downfall of the current study was the use of an open randomized technique during patient recruitment. As a result when we compared both groups, it was evident that in the study group secondary infertile patients outnumbered primary infertile couples, whereas in the control group primarily infertile patients were more common

Conclusion

To conclude, results of this study revealed that perturbation prior to insemination does affect pregnancy rates with no statistical difference seen in the saline group as well as lidocaine group. However total clinical pregnancy rate was found to be a little more in the lidocaine group than the saline group.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors

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Comment [S28]: Reference must be revised and typed according to style recommended by journal

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Comment [S29]: Examples for references style correction
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