HYSTEROSCOPIC TUBAL OCCLUSION USING ISO-AMYL-2-CYANOACRYLATE MIXED WITH ETHIODIZED OIL (LIPIODOL) IN PATIENTS WITH HYDROSALPINX

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Abstract

Background: Before using IVF, a laparoscopic salpingectomy is performed. This invasive surgery carries a considerable risk when performed on patients who have large intra-abdominal adhesions. In addition, it might interfere with the blood flow to the ovaries, which would lower their reserve.

Aim of the Work: to assess the efficacy of using Iso-amyl-2-cyanoacrylate mixed with Ethiodized oil (Lipiodol) as a new method for tubal occlusion among infertile women with hydrosalpinx.

Patients and Methods: From June 2020 to April 2023, this pilot study was carried out at the Department of Obstetrics and Gynecology, Ain Shams Faculty of Medicine, Early Cancer Detection and Hysteroscopy Unit at the Ain Shams Maternity Hospital. In order to prevent Amcrylate from solidifying or turning into crystals, 0.5 mL (one ampoule) of iso-amyl-2 cyanoacrylate (Amcrylate) was injected with 0.5 ml of lipiodol dye in the same syringe for a hysteroscopic tubal occlusion using Bettocchi rigid office hysteroscopy without anesthesia. This procedure was performed on 25 women who had been diagnosed with unilateral or bilateral hydrosalpinx and were prepared for IVF.

Results: Regarding success rate, our study reported that among total of 25 cases, hysteroscopic tubal occlusion succeeded in 14 women (56%) in whom 16 tubes (57.1%) were successfully occluded, (14 tubes were occluded after the first trial and remaining 2 tubes were after the second trial). Regarding postoperative complications, pain was reported, 11 women (44%) felt mild pain and 14 women (56%) felt no pain. Also, mild vaginal bleeding was reported by all women 100%. However mild fever was reported by 5 women (20%) only.

Conclusion: It is safe and successful to utilize iso-amyl-2-cyanoacrylate combined with ethiodized oil for hysteroscopic tubal occlusion in individuals with hydrosalpinx. It had a 56% success rate and only a few post-procedural side effects, such as discomfort, bleeding, and fever, were noted. This work adds to the body of knowledge and provides some insight for anticipated future research with larger sample sizes to reevaluate our conclusions.

Key words: hysteroscopic tubal occlusion, Iso-amyl-2-Cyanoacrylate, ethiodized Oil, lipiodol hydrosalpinx

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INTRODUCTION

A complicated condition with important medical, psychological, and financial ramifications is infertility. Significant progress has been made in the treatment of infertility. especially the advancement of technology for assisted reproduction (ART). The process known as in vitro fertilization (IVF) is intended to treat infertility and result in pregnancy as a direct consequence of the intervention. ***(Hasanpoor-Azghdy et al., 2014).{1}***

Usually the outcome of a prior pelvic infection, such as pelvic inflammatory disease, tubal obstruction and tubal infertility can also be brought on by endometriosis and other disorders. Distal tubal occlusion, which affects the end that faces the ovary, is frequently brought on by Chlamydia trachomatis and is usually linked to the development of hydrosalpinx. Such an infection may be linked to pelvic adhesions. The fimbriae may become agglutinated and damaged in less severe cases. ***(Patil, 2009).{2}***

Following the resolution of PID, the injured fallopian tube may expand, get obstructed, or fill with sterile fluid. Another cause of hydrosalpinx is damage to the fallopian tube from prior surgery or adhesions. ***(Carter and Garmel, 2016).{3}***

Numerous research investigations have illustrated the adverse effects of hydrosalpinx on the incidence of conception, implantation, premature miscarriage, preterm birth, and live birth in individuals undergoing in vitro fertilization (IVF). ***(Chua et al., 2017).{4}***

The leakage of hydrosalpngeal fluid from the tube into the uterine cavity may impede implantation either by flushing the embryos out of the cavity or disrupting the endometrium at the implantation site. Furthermore, hydrosalpinx fluid contains microorganisms,debris, toxins, cytokines, and

prostaglandins that may impair endometrial receptivity and possibly reduce the percentage of motile spermatozoa ***(Lu et al., 2013).{5}***

IVF is advised as the first line of treatment for women with severe tubal disease (bilateral hydrosalpinx, both proximal and distal blockage, substantial adhesions), as tubal surgery is unlikely to be beneficial in these patients. For best results, hydrosalpinx should be eliminated before IVF. ***(Chua et al., 2017).{4}***

Before using IVF, a laparoscopic salpingectomy is performed. This invasive surgery carries a considerable risk when performed on patients who have large intra-abdominal adhesions. In addition, it might interfere with the blood flow to the ovaries, which would lower their reserve. Although laparoscopic proximal tubal occlusion has shown encouraging results, it still requires abdominal and pelvic cavity entrance, which carries a certain amount of risk. ***(Yu et al., 2019).{6}***

A great deal of work has gone into creating noninvasive techniques for tubal occlusion that use the right mechanical or chemical agent. Before IVF, hysteroscopic proximal tubal blockage using Essure microinsert seems to be a viable choice for patients with hydrosalpinx. Regretfully, it was discovered to be linked to difficulties and a high miscarriage rate (withdrawn from the market). A study on the impact of hysteroscopic rollerball coagulation for proximal tubal occlusion was carried out in a low-resource context; however, the authors did not investigate the impact of this operation on the rate of implantation in IVF-ET cases ***(Legendre et al., 2013).~{7}***

However, the majority of noninvasive methods resulted in either severe side effects or inadequate tubal occlusion. Recently, a safe and efficient technique for hysteroscopic uterine tube blockage was discovered with the application of cyanoacrylates (Cas), sclerosing agents. A derivative of CA, iso-amyl-2-cyanoacrylate has been successfully utilized recently to treat bleeding esophageal varices, gastric Dieulafoy's lesion, and clog digestive, urinary, and pulmonary fistulas without causing major side effects. Advanced gamma sterilized, non-pigmented, non-toxic, non-allergic, bio-static tissue adhesive that is also bacteriostatic and hemostatic is called iso-Amyl 2-Acrylate. In addition to being easy to apply and safe, it permits quick wound closure with little scarring, lowers the risk of infection and trauma following surgery, does not react to the tissues or get absorbed in the blood, and causes less granuloma and oedema formation than sutures ***(Amer et al., 2018).{8}***

Side effects of Iso-Amyl 2-Cyano Acryate are:

Iso-Amyl 2-Cyano Acrylate's metabolites, cyano acetate and formadehude, can induce an inflammatory reaction in the tissues around them. **(Thomas, 2001)"9"**

Rat Histotoxicity of Cyanoacrylate Tissue Adhesive: Subcutaneous hepatic and marrow cavity implant sites were used to compare the histotoxic characteristics of methyle-, hexyl-, and decyl-2-cyanoacrylate polymers. While the two larger molecular weight homologues caused a foreign-body granuloma response preceded by transitory inflammation, methyl-2-cyanoacrylate was highly necrotizing and pyogenic **(Woodward et al., 1964)."10"**

The purpose of this study is to evaluate the effectiveness of a novel technique for tubal occlusion in infertile women with hydrosalpinx: iso-amyl-2-cyanoacrylate combined with ethiodized oil (lipiodol.)

PATIENTS AND METHODS

The current prospective interventional pilot study involved 25 women who met the following criteria: they were diagnosed with hysteron-salpingography (HSG) as having unilateral or bilateral hydrosalpinx, attended an outpatient clinic for infertility treatment and follow-up, and had tubal factor of infertility. The study was conducted from June 2020 to April 2023 at the Early Cancer Detection and Hysteroscopy Unit of the Ain Shams Maternity Hospital - Department of Obstetrics and Gynecology, Ain Shams Faculty of Medicine.

Exclusion criteria:

Any patient with a history suggestive of :

- Acute pelvic inflammatory disease.
- Endometritis.
- Lower genital tract infection.
- The presence of intrauterine synechiae.
- Presence of uterine anomalies as uterine septum or a submucous fibroid located near or at the cornu of the uterus.
- Undiagnosed genital bleeding.
- Any suspicion of pregnancy.
- Any suspicion of malignancy.

Sample size justification:

Ethical considerations:

- Information about the patient and informed consent: the patient gave her assent to participate in the clinical trial prior to enrollment after being given a clear explanation of its purpose, scope, and potential drawbacks.
- Confidentiality: The investigators retained any documents containing the patient's name in a safe location. Only the patient's initials were entered into the case report form. To make records identifiable, the scientists kept a personal patient identification list, which included patient initials matched to corresponding patient names.
- Protocol approval: the OB/GYN department council at Ain Shams University deemed the protocol and all related documentation to be ethical and research approved prior to the start of the study and in compliance with any local regulations followed.

- Regarding efficacy and safety, there is no proof that study interventions had any significant negative consequences.

Study interventions and procedures:

- Hysterosalpingography (HSG) was used to diagnose unilateral or bilateral hydrosalpinx in 25 women with tubal factor of infertility for the purpose of this study.

- • The treatment plan for each patient included hysteroscopic tubal occlusion of hydrosalpinx.

- • Before completing an informed permission form, the patients received counseling and had any doubts about the procedure's safety or the type of chemical used addressed.

All cases were subjected to:

- **Full history taking:** careful history taking including obstetric history and gynecological history with determination the causes of infertility and hysterosalpingographic finding of hydrosalpinx.

- **Physical examination:**
  - **General examination:** including the vital data (pulse, blood pressure and temperature).
  - **Abdominal examination:** for previous abdominal scars.

- **Pelvic examination including:**
  - Sterile speculum examination for detection of any cervical pathology or vaginal bleeding.
  - Digital pelvic examination for assessment of cervical mass, tenderness, mobility and any other pelvic pathology.

Investigations:

- **Ultrasound examination:**

Transvaginal sonography was performed for assessment of uterine or adnexal abnormalities using Mindray DP-15 Digital Ultrasonic Diagnostic Imaging System and GE Logiq E9 ultrasound machine, 2–5 MHz transvaginal, curved array transducer.

- **Hysterosalpingograghy**: for assessment of uterine cavity and tubal patency or pathology.
- **Infertility work up**: including baseline day 2 female hormonal profile (FSH, LH, E2, TSH, AMH, serum prolactin) and semen analysis.
- **Previous hysteroscopic** assessment to exclude any pathology hindering the procedure.

- **Protocol of study: Instrumentation:**

1- The research involved 25 females who had tubal fibroids.1. Bettocchi endomat infusion, model 26 33 10 20, with a 300 ml/min infusion rate, 100–120 mm Hg of pressure, and 0.2 suction
2- Fibroptic light: 150-watt Xenon nova, model 20 13 15 20 made by Storz
3- Hysteroscopic apparatus (Germany, Karl Storz, Tuttlingen)
4- telescope: stiff, utilizing a Hopkins 11 lens system, 30° Bettocchi type 26157 BT. The sheath features a 2.9mm rodlens and an operating channel for the instrument employed, 26163 V, with an outer diameter of 5 mm.
5- Camera: TV DX buddy model 20 23 20 20 by Storz, Karl Storz-endoscope
6- Fifth, semi-rigid and semi-flexible instruments
7- Collen prepared his tenaculum, speculum, and sound for use as needed.
8- TVCR Goldstar, model NO.KKV-9050, 50/HZ, AC 100-270 V, monitors the hysteroscopic event tor of infertility, as determined by hysterosalpingography (HSG), with either unilateral or bilateral hydrosalpinx.
9- The treatment plan for each patient included hysteroscopic tubal occlusion of hydrosalpinx.
10- Before completing an informed permission form, the patients received counseling and had any doubts about the procedure's safety or the type of chemical used addressed.

Pre-Hysteroscopy medications:

One day prior to the hysteroscopy, each patient received two 500 mg tablets of Metronidazole (Flagyl) and one 500 mg tablet of Levofloxacin (TAVANIC). Four days following the injection, the prescribed regimen was one 500 mg tablet of Levofloxacin taken daily and one 500 mg tablet of Metronidazole taken every twelve hours. Prior to hysteroscopy, they were administered with a single 150 mg dose of Ketoprofen rectal suppository (Profenid).

C-Technique:

- With or without anesthetic, all hysteroscopic procedures were performed during the early follicular phase (cycle days: 4–10).
- After lying in the dorsal lithotomy position, the patient was sterilely prepared and draped. The patient's thighs are positioned 90 degrees from the pelvis to provide for adequate room for hysteroscope manipulation. The patient's sacrum and coccyx are supported on the table's flat surface, and their perineum extends slightly beyond its edge.
- To prepare the vagina, povidone-iodine (Betadine) was used.
- A vaginal examination was done to look for any adnexal lumps as well as the uterus's size and axis.
- Instead of using the vaginal introitus, the tip of the hysterosope was positioned there (Bettocchi's vaginaloscopic method). The vagina swelled up with salt.
- The scope was advanced to the internal os and the uterine cavity after being slowly pushed backwards to detect the external cervical os, which could be easily seen when the posterior fornix was reached.

- A strict Bettocchi office In every instance, a 5-mm-diameter hysteroscope with a 30-degree 2.9-mm telescope and a 5F working channel was employed.
- A Bettocchi Hysteromat was utilized to automatically adjust intrauterine pressure between 100 and 120 mm Hg while using diluted water or normal saline as a distension medium.
- Using a 4 Fr, 42-cm long polyethylene ureteric catheter with terminal opening (Amecath company), the proximal 1 cm of the tube with hydrosalpinx was cannulated in each patient through the side channel of the hysteroscopy. Here, 0.5 mL (one ampoule) of iso-amyl-2 cyanoacrylate (Amcrylate) (Figure 6) was combined with 0.5 ml of lipiodol dye (Figure 7) in the same syringe to prevent Amcrylate from solidifying or turning into crystals when injected.
- In order to guarantee intratubal injection of the entire dosage, 0.7 of normal saline was injected right after the injection of lipiodol and isoamyl-2-cyanoacrylate into the afflicted tube.

Post-Hysteroscopy procedures:

- The patients were discharged with instructions to return right away to the hospital in the event that they experience fever, abnormal vaginal discharge, or abdominal or pelvic pain. • The patients were kept under observation for one hour following injection in order to collect vital signs and assess abdominal pain and tenderness. If not, patients were supposed to return one or three months after the injection to verify total tubal blockage by HSG.
- After one month of the initial injection, patients with incomplete tubal occlusion (partial occlusion) or unoccluded tubes had reinjection with iso-amyl-2-cyanoacrylate. Two months later, HSG was performed to establish full tubal occlusion.

Consent:

- A hysteroscopy procedure will be done for you as a part of research in which we assess the efficacy of hysteroscopic tubal occlusion using 1/2 ml of chemical substance (Amcrylate) mixed with (lipiodol) which are known to be safe from the medical point of view.
- There are no known major side effects or complications to the use of these substances, only sometimes you may feel mild lower abdominal pain just after injecting the substance, (and this is due to the thermal effect of Amcrylate) for which you will receive oral or rectal analgesic before the procedure.
- You will be under observation for abdominal pain or fever for the first few hours after the procedure.
- You will receive prophylactic antibiotic for one day pre injection and four days post injection to avoid flaring of any hidden infection in the tubes
- Follow-up by HSG will be done one and three months post-procedure to be sure of complete occlusion of the tubes.

Patient name and signature:

Patient identity card number:

Study outcomes:

Primary outcome: The efficacy of the procedure was measured by hysterosalpingogram which was done one and three months later after procedure to assess the success of tubal block by Iso-amyl-2-cyano Acrylate mixed with ethiodized oil (Lipiodol).

Secondary outcomes: The safety of the procedure was measured clinically by putting the patient under observation for abdominal pain or fever for the first few hours after procedure.

Statistical analysis:

The statistical software for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA), was used to analyze the recorded data. Standard deviation (SD) was used to represent quantitative data as mean ± SD. Frequency and percentage were used to convey qualitative data. Fisher's exact test was used in place of the Chi-square test for group comparisons using qualitative data where the predicted count in any given cell was less than 5. The allowable margin of error was set at 5%, while the confidence interval was set at 95%. Consequently, the p-value was deemed significant since the subsequent P-value <0.05 was deemed significant.

RESULTS

Table (1): Baseline characteristics distribution among study group (n=25).

Baseline characteristics	Total (n=25)
Age (years)	
Mean±SD	(33.72±4.79)
Range	25-43
BMI [wt/ (ht)^2]	
Mean±SD	27.34±2.92
Range	21.8-33.2
Obesity	
Normalweight	4 (16.0%)
Obese	6 (24.0%)
Overweight	15 (60.0%)
Duration of marriage (yrs)	
Mean±SD	8.32±3.34
Range	1-14
Previous ICSI/IVF	
No	10 (40.0%)
Once	4 (16.0%)
Twice	4 (16.0%)
Thrice	2 (8.0%)
4 Times	3 (12.0%)
5 Times	2 (8.0%)

Table (1): The study was conducted on a wide age group ranging from 25 to 43 years, (mean age of 33.72±4.79 years).

Table (1) and Figure (9): The mean BMI was 27.34±2.92; while 6 patients (24%) were obese; as for the duration of marriage ranged from 1 to 14 years with mean 8.32±3.34.

Table (1) and Figure (10): As for previous ICSI/IVF: 4 women (16.0%) had previously undergone ICSI/IVF once, 4 women (16.0%) had undergone it twice, 2 women (8.0%) thrice, 3 women (12.0%) : 4 times and 2 women (8.0%) : 5 times.

Table (2): Infertility distribution among study group (n=25).

Infertility	Total (n=25)
Duration of Infertility (yrs)	
Mean±SD	7.00±3.12
Range	1-13
Type of Infertility	
Secondary Infertility	17 (68.0%)
Primary Infertility	8 (32.0%)
Cause of Infertility	
Tubal factor	25 (100.0%)

Table (2) and Figure (11): The mean duration of infertility “years” was 7.00±3.12; as for type of infertility : 17 women (68%) were complaining of Secondary infertility and 8 women (32%) were complaining of primary infertility, the cause of infertility is tubal factor in all women (100%).

Table (3): Anesthesia and type of anesthesia distribution among study group (n=25).

	No.	%
Anesthesia		
None	11	44.0%
Yes	14	56.0%
Type of Anesthesia (n=14)		
General	10	71.4%
Spinal	4	28.6%

Table (3) and Figure (12 &13): Show that there were 14 women (56%) underwent the procedure under anesthesia, 10 women (71.4%) out of them had general anesthesia and 4 women (28.6%) had spinal anesthesia.

Table (4): Tubal occlusion after one and two times injection of Iso-amyl- 2-cyanoacrylate mixed with Ethiodized oil as diagnosed with HSG (n=25).

Results Outcome by HSG	No.	%
***Total number of cases**	25	100.0%
No. of cases failed occlusion	11	44.0%
Total No. of successful cases	14	56.0%
#No. of tubes injected	28	100.0%
No. of tubes Failed occlusion	12	42.9%
Total No. of tubes occluded	16	57.1%
After the first injection	14	50.0%
After the second injection	2	7.1%

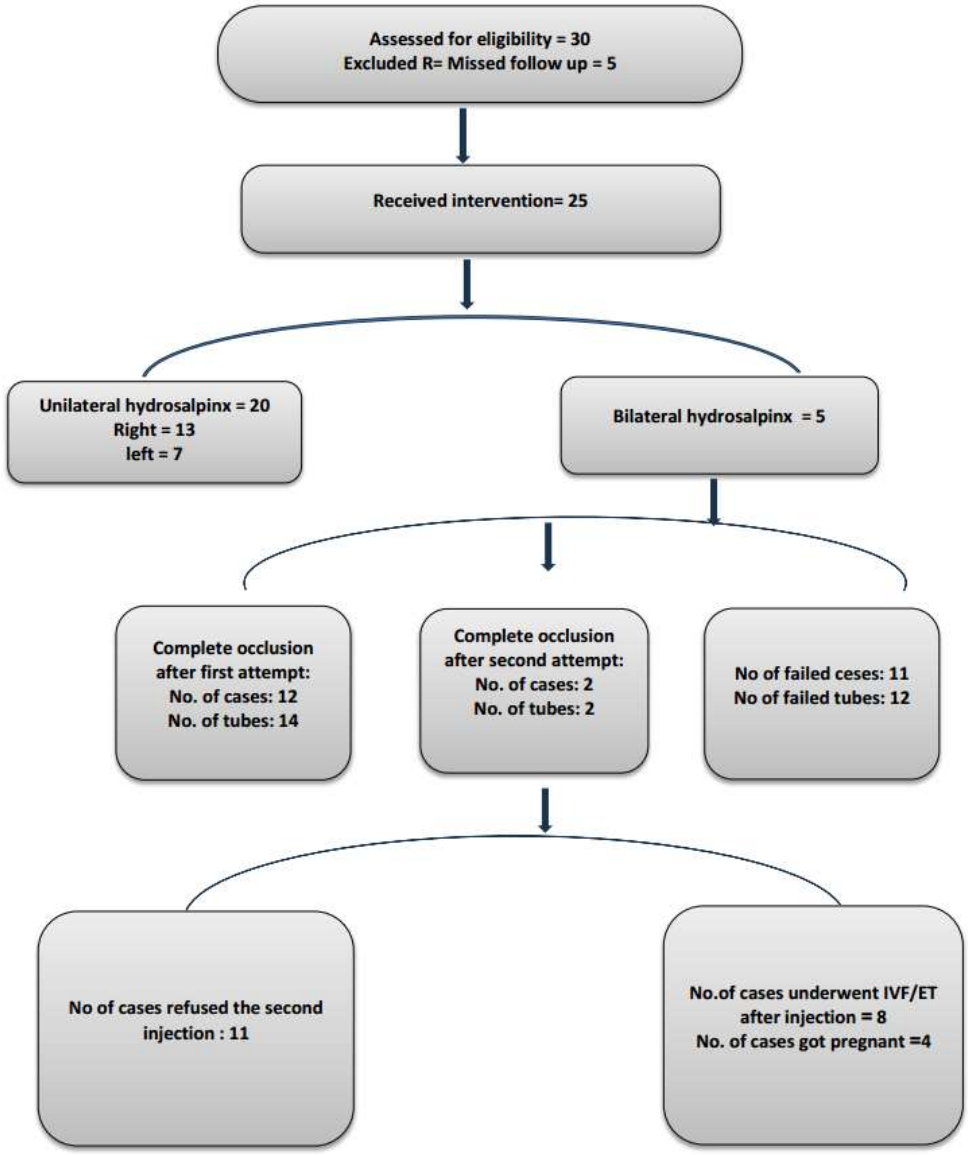
**Percentage of cases from total of cases*
#Percentage of tubes from total of tubes

Table (4) and figure (14&15): Results outcome by HSG for total number of cases: 11 women (44%) were failed cases, and 14 women (56%) were successful cases among study group.

Finally, results outcome by HSG for number of tubes injected: 12 tubes (42.9%) were failed and 16 tubes (57.1%) were successfully occluded, (14 tubes out of them were after the first time and 2 tubes were after the second time)

Table(5): Tubal occlusion by hysterosalpingography 1 and 3 months after Iso-Amyl-2-cyanoacrylate in unilateral and bilateral patients.

Hydrosalpinx in tubes by HSG	Total patients (n=25)	Complete occlusion after first injection	Complete occlusion after second injection
Right	13	7 (53.8%)	1 (7.7%)
Left	7	5 (71.4%)	0 (0.0%)
Bilateral			
Rt.	5	1 (20.0%)	0 (0.0%)
Lt.	5	1 (20.0%)	1 (20.0%)
Total	28	14 (50.0%)	2 (7.1%)



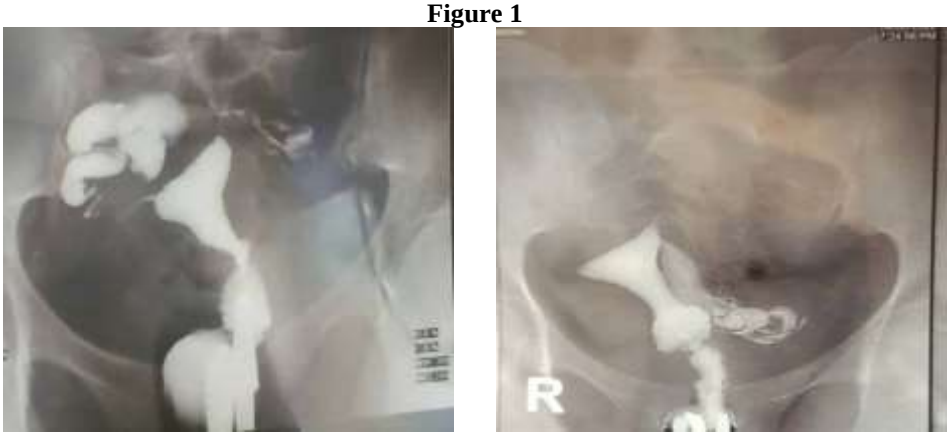
Flow chart results outcome by HSG distribution among study group.

Table (6): Postoperative complications distribution among study group (n=25).

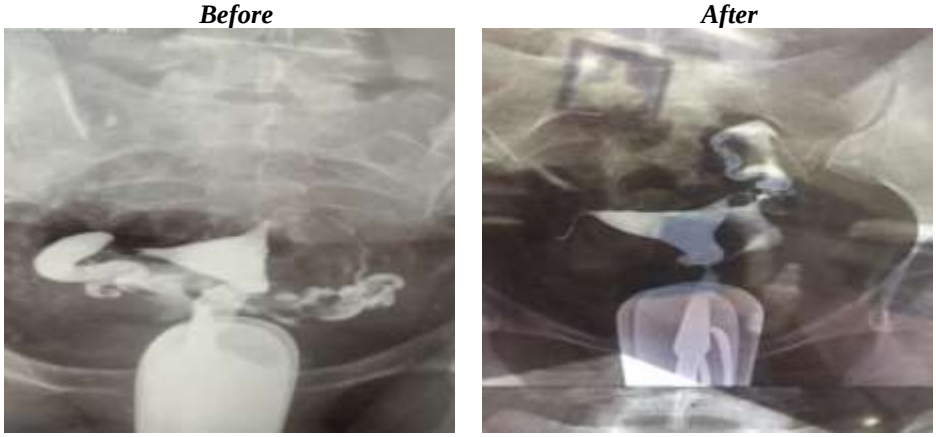
Postoperative complications	No.	%
Pain		
None	14	56.0%
Mild	11	44.0%
Bleeding		
Minimal	25	100.0%
Fever		
Mild	5	20.0%
No	20	80.0%

Postoperative complications: As for pain: 11 women (44%) felt mild pain and 14 women (56%) felt mild pain. As for bleeding : all women had minimal bleeding 100%. As for fever: 5 women (20%) had mild fever.

Figure 1



Before ***After***



Before ***After***

DISCUSSION

Before IVF, hysteroscopic proximal tubal blockage with an Essure micro-insert seems to be a viable choice for patients with hydrosalpinx. Regretfully, it was shown to be linked to difficulties and a high miscarriage rate. (Barbosa and others, 2016a)"11" (hence, taken off the market)

To the best of our knowledge, **there are no studies in literature** assessing our study outcomes and most of studies that disagreed with our results were due to several causes as different study methodology, outcomes, sample size and different medical conditions of studied cases at time of enrollment.

Regarding **success rate**, our study reported that among total of 30 cases, 5 cases didn't follow-up (**missed cases**), 25 cases followed-up. Hysteroscopic tubal occlusion succeeded in **14 women (56%)** in whom **16 tubes (57.1%)** were successfully occluded, (**14 tubes** were occluded after the first trial and remaining **2 tubes** were after the second trial).

Regarding **postoperative symptoms**, **pain was reported in all cases** shortly after injection due to the thermal effects of Amcrylate, 11 women (44%) felt mild pain and 14 women (56%) felt no pain. Also, **mild vaginal bleeding** was reported by all women 100%. However mild **fever** was reported by **5 women (20%)** only.

Amer et ala {12} evaluated infertile patients with hydrosalpinx in 2018 before undergoing in vitro fertilization (IVF) to determine the efficacy of hysteroscopic tubal occlusion using iso-amyl-2-cyanoacrylate. Forty infertile women preparing for experimental vitro fertilization had 0.5 mL of isoamyl-2-cyanoacrylate injected hysteroscopically into their fallopian tubes using hydrosalpinx. Following one or three months, the patients underwent hysterosalpingography (HSG) to ensure total tubal blockage. They stated that it is safe and successful to utilize iso-amyl-2-cyanoacrylate for hysteroscopic tubal occlusion in patients who had hydrosalpinx before IVF. Out of the 54 tubes that were injected in this study, 42 (77.8%) were fully occluded after a single injection, while 12 (22.2%) were only partially occluded. After the partially occluded tubes were reinjected, the HSG of every patient revealed that, three months after the initial injection, 48 (88.9%) of the tubes had fully occluded while 6 (11.1%) were still partially occluded. Eight patients (20%) did not show up for follow-up, while thirty-two patients (80%) had one IVF/ET cycle. Of the patients that had IVF/ET, 24 (75%) were pregnant, while 8 (25%) were unable to conceive. Of the pregnant patients, 13 (54.2%) did not

give birth yet, 3 (12.5%) had first trimester abortions, and 8 (33.3%) gave birth at term.

A single hysteroscopic tubal injection of iso-amyl-2-cyanoacrylate results in an instantaneous tubal block in 80% of instances in the Amer et alb {12} trial, without causing a substantial inflammatory reaction, mucosal necrosis, or intramural fibrosis. The only adverse reaction was a slight lower stomach ache that last for less than five minutes following the injection; no further side effects were experienced due to annoyance or irritation. The attempt to accomplish the procedure was unsuccessful in eighteen cases when the tubal cannulation was impeded by intracavitary lesions .

A cyano-acrylate derivative (CA) was utilized in the Amer et alb {12} study. These materials have been safely and successfully applied in a variety of medical indications, such as blocking digestive tract flow, urinary tract blockage (Muto et al., 2005{13} study), pulmonary fistulas (Cagirici et al., 2007{14} study), wound, laceration, and corneal ulcer healing, mesh fixation for inguinal hernia (Jourdan and Bailey, 1998) {15} study, adhesion of bone or cartilage (Kim, 1997 {17} study), and controlling bleeding from esophageal varices (Tan et al., 2006 {18} and Qiao et al., 2015 {19} studies.(

When CA comes into contact with moisture, it transforms into an inert polymer, which solidifies quickly in 5–10 seconds and fixes in a minute, according to a 2002 study by Maartense et al. {20.{

According to Devrukhkar et al. (2015) {21}, cyanoacrylate tissue adhesive is bacteriostatic and incredibly adhesive to biological tissue, making it advantageous when used to occlude hydrosalpinx prior to IVF. A study was carried out to assess the advantages of cyanoacrylate tissue adhesive as an alternative to suturing in the management of pediatric lacerations.

Higher cyanoacrylates, such as N-butyl-2-cyanoacrylate and iso-amyl-2-cyanoacrylate, are less histotoxic and have no carcinogenic effects, but they degrade more slowly than those with shorter side chains. These benefits of using cyanoacrylate adhesives were reported by Samuel et al. {22} in 1997 and Nagpal et al. {23} in 2004.

According to a 1959 study by Coover et al. {24}, the polymerization of CA is exothermic, and the heat produced could account for the moderate discomfort that all patients experienced right after injection.

Edmonson {9} reported in 2001 that in addition to the local anesthetic effect of the formaldehyde making the patient's pain after injection mild, the metabolites of iso-amyl-2-cyanoacrylate (cyanoacetate and formaldehyde) cause inflammation in surrounding tissues, which would aid in long-term tubal occlusion.

In the Amer et al. {13} investigation, the histopathology of the blocked tubes revealed plicae aggregation, minor stromal inflammation, but no serosal involvement—with the exception of two cases that went unreported clinically, one of which had an Amacryl plug ejected freely in the Douglas pouch. Examining the hysteroscopic record of the previous patient revealed the presence of a submucous fibroid, requiring more ureteric catheter manipulation and forcing. This likely resulted in a greater force being utilized to inject the isoamyl-2-cyanoacrylate and its ejection to Douglas Pouch.

According to Bigolin et al. (2009), there was a comparable action of n-butylacrylate on the tubal epithelium of an animal model, resulting in the production of an acrylic plug that blocked the tubal lumen without harming the epithelium. "25"

In two of the cases reported in the single human report employing n-butyl cyanoacrylate, the CA was injected by radiologic guided fluoroscopic cannulation of the tubes. Two years of follow-up on these instances verified the tubal blockage, however Pelage et al. (1998) did not do any histology."26"

The use of methyl cyanoacrylate (MCA) as a sclerosing agent in conjunction with transvaginal microcatheterization techniques to evaluate a nonsurgical, nonhormonal sterilization procedure, on the other hand, revealed a severe tissue reaction with necrosis, according to a report by Berkey et al in (1995).In 1972 and 1986, respectively, Stevenson and Taylor{28} and Guzman-Serani et al {29} reported that in humans, 40% of patients experienced a decrease in menstrual blood volume after methyl cyanoacrylate was applied to the Femcept device for tubal occlusion. This could have been caused by a severe tissue reaction resulting in endometrial damage.

However, in addition to their high cost and the nickel allergy associated with Essure, the usage of Adiana® silicon inserts and Essure® micro inserts has been linked to severe inflammation and fibrosis in the uterine tube, as described by Basinski in 2010.{30} (i.e., taken off the market(

Through the formation of an acrylate plug and the amalgamation of tubal plicae, iso-amyl-2-cyanoacrylate produces instantaneous tubal occlusion; however, complete tubal occlusion after a fissure must wait three months. In addition, as IVF is an inert substance, it won't alter the uterine cavity's interior environment in women with hydrosalpinx, which means it won't negatively impact any existing pregnancies that may arise. Since the injection is a low-cost office procedure, it could be repeated until HSG confirms tubal blockage .

women with hysterectomy indications should be the ones to evaluate the tissue effect and safety of iso-amyl-2-cyanoacrylate in the fallopian tubes; however, this is only practical for women who have finished their families. In the Amer et alb {13} study, every case had concurrent uterine disease; hence, it would be easier to perform tubal cannulation and achieve efficient tubal occlusion if the occlusion was done in a healthy uterus, such as in cases of

sterilization or hydrosalpinx before IVF. This is a challenging topic to address because we believe that the type of concurrent uterine pathology may have an impact on the degree of occlusion; in this study, patients with adenomyosis or fibroid uterus had a higher failure rate (3 out of 13 and 2 out of 5, respectively), compared to 1 out of 7 cases with endometrial hyperplasia .

While methylene blue testing is the gold standard for tubal patency, the primary purpose of the histopathology in the Amer et alb {13} study was to evaluate the tissue effect of iso-amyl-2-cyanoacrylate rather than tubal occlusion. The low number of occluded tubes at histopathology may have resulted from processing and tube distortion during sectioning. Extended follow-up to confirm appropriate tissue reactions may lead to a higher proportion of cases of complete tubal blockage. This was not possible in the Amer et alb {13} trial, as all patients had uterine pathology requiring treatment .

According to reports by Cooper et al. in 2003 {31} and Levie and Chudnoff in 2005, silicone implants, hydrogel dispositive, metallic embolus, endometrial ablation using laser, diode, or radio-frequency, sclerosing substances, or adherence fibrin, did not prove to be safe for routine use in hysteroscopic occlusion.

According to a 2010 study by Beerthuizen, the use of either electrocoagulation or macrolide antibiotics (erythromycin tablets) was linked to a high failure rate in more than 35% of cases, with potentially serious complications in the later stages due to heat transfer or unintentional tubal perforation that caused damage to the adjacent bowel. "32"

The Adiana (Adiana, Redwood City, CA) and Essure® (Conceptus, Inc., San Carlos, CA) are two mechanical devices that, when placed inside the tube, cause granulomatosis tissue to form as well as a complete occlusion in three months. According to Hastings-Tolsma et al. (2006), the Essure® is the only dispositive that has been approved by the European Health Office (EHO) and the Food and Drug Administration (FDA)."33"

In 2014, Edmonton {9} finally announced that, in addition to its exorbitant cost, notable adverse events related to the use of Essure® included expulsion, perforation of the Fallopian tubes, migration of the device to the abdominal cavity, and vasovagal responses. As a result, the device was pulled from the market and is no longer in use.

CONCLUSION

From our study we can conclude that iso-amyl-2-cyanoacrylate mixed with Ethiodized oil used for hysteroscopic tubal occlusion in patients with hydrosalpinx prior to IVF is safe and effective. Its successes rate was 56% with minimal reported post procedure adverse effects as pain, bleeding and fever. The present study can burden the knowledge and shed some light on future prospective studies with larger sample sizes to reassess our findings.

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