

Hysteroscopic Tubal Occlusion with the use of Iso-Amyl-2-Cyanoacrylate

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ABSTRACT

Objective: To assess the safety and effectiveness of using Iso-Amyl-2-cyanoacrylate for hysteroscopic tubal occlusion in women.

Methods: It is a pilot study on 25 patients with benign uterine lesions indicates hysterectomy. Hysteroscopy tubal injection of 0.5 ml Iso-amyl-2-cyanoacrylate was done in one tube of each patient and the other tube was used as a control. The Patients were then randomly scheduled for total abdominal hysterectomy and bilateral salpingoophorectomy into 5 equal groups: Group 1 was scheduled first day post hysteroscopy, Group 2 after one week, Group 3 after 2 weeks, group 4 after 3 weeks and group 5 after 4 weeks. Methylene blue test on the hysterectomy samples for tubal patency and histopathology for severity of tissue reaction was done. Categorical variables were presented as number and percentage and intergroup differences were compared using Fisher's exact test. P-value <0.05 was considered statistically significant.

Results: Tubal chronic nonspecific inflammation was noted in all cases and perisalpingitis was noted in two cases (8%). Twenty cases out of 25 had a negative methylene blue test representing an 80% success rate for tubal occlusion. All cases were occluded in Group 1, in groups 2, 3 and 4 each had four cases (80%) and group 5 had three cases (60%) with tubal occlusion, without statistically significant difference between the five groups.

Conclusion: Iso-amyl-2-cyanoacrylate for hysteroscopy tubal occlusion is safe, while evaluation of its effectiveness for sterilization will still require a larger sample size and a longer period of follow up.

Keywords: Fallopian tube, hysteroscopy, Isoamyl-2-cyanoacrylate.

INTRODUCTION

Tubal occlusion via laparoscopy or minilaparotomy is the most widely used technique of sterilization in women with the risk of vascular or other organ injury, the development of peritoneal adhesions and the risk of anesthesia^{1,2}. In addition, surgical techniques are typically more expensive than less invasive nonsurgical methods³. Several studies have long demonstrated negative consequences of hydrosalpinx on the rates of pregnancy, implantation, early pregnancy loss, preterm birth, and live delivery in patients undergoing in vitro fertilization (IVF).^{4,5} Laparoscopic salpingectomy before IVF has been demonstrated to restore outcomes, but is invasive and is associated with higher risk in

patients with significant intra-abdominal adhesions and may disturb the ovarian blood supply resulting in a reduced ovarian reserve^{6,7}. Results of laparoscopic proximal tubal occlusion have been promising, but this approach also involves entry into the abdominopelvic cavity with its inherent risk⁸.

Therefore, considerable effort is being devoted to the development of noninvasive methods of tubal occlusion with the use of a suitable mechanical or chemical agent. Mechanical devices like coils, micro spindles⁹, silicon plugs¹⁰, and hydrogel are inert and occlude or stretch the lumen of the tube, obstructing ovum or sperm passage¹¹. Chemical agents include ethanol, tetracycline, quinacrine hydrochloride, and sclerosing agents^{12, 13,14,15,16}. Nevertheless,

most noninvasive techniques do not produce satisfactory tubal occlusion and/or produce serious side effects. The recent exception is the use of cyanoacrylates, sclerosing agents, which was found to be a safe and effective method of hysteroscopic uterine tube occlusion in rabbit.^{13,16} Iso-amyl-2-cyanoacrylate is a cyanoacrylate derivative recently used successfully in obstructing digestive, urinary and pulmonary fistulas and for management of bleeding esophageal varices and gastric Dieulafoy's lesion without serious complications.^{17,18,19,20}

More recently, hysteroscopic proximal tubal occlusion by Essure® micro insert (Conceptus, Inc., Mountain View, CA) appears to be an effective alternative in women for contraception and before IVF in those with hydrosalpinx²¹. In a low resource setting a trial was conducted to effect proximal tubal occlusion by hysteroscopic roller ball coagulation, but the effect of such a procedure on the rate of implantation in cases of IVF-ET is not followed by the authors²².

This pilot study is aimed to assess the safety and effectiveness of hysteroscopic tubal occlusion using Iso-Amyl-2-cyanoacrylate in women, which would make it an easy office procedure for cases with hydrosalpinx prior to IVF and for tubal sterilization.

MATERIALS AND METHODS

This study was conducted in the Endoscopy Unit of Ain Shams University Maternity Hospital, Cairo, Egypt after approval of the ethical committee and according to the guidelines of the 1975 Declaration of Helsinki on human experimentation. It admits 25 patients who were scheduled for total abdominal hysterectomy and bilateral salpingo-oophorectomy for benign uterine lesions. Patients with a history of / or ongoing pelvic inflammatory disease, infertility or pelvic surgery were excluded. Questions concerning the safety of the procedure and the chemical used were answered before signing an informed consent.

Hysteroscopic Procedure

All patients were pre-medicated with 150 mg Ketoprofen rectal suppositories (Profenid® - Sanofi-Aventis Pharma) one hour before hysteroscopy. A Bettocchi rigid office Hysteroscope, of 5 mm diameter, based on a 2.9-mm telescope 30o with a 5F operating channel (Karl Storz GmbH & Co. KG, Tuttlingen, Germany), was used in all cases.

Isotonic normal saline 0.9% was used as a distension medium with intrauterine pressure between 100 and 120 mm Hg controlled automatically using a Hamou Hysteromat (Karl Storz GmbH & Co KB).

Cannulation of the proximal one centimeter of the Fallopian tube was done using a 4 Fr, 42cm long, a polyethylene ureteric catheter with terminal tip (Bard Medical Inc. - Covington, GA; USA), through the side channel of the hysteroscope, where 0.5 ml (one ampoule) of Iso-Amyl-2-cyanoacrylate (AMCRYLATE® Concord Drugs Ltd., Hyderabad; India) was injected at one tube in each patient and the other tube was used as a control, not cannulated and no material was injected into it²³. The patients were kept under observation for one hour after injection and then were transferred to her ward and observed for 24 hours for vital data, abdominal pain and tenderness.

The Patients were then randomly scheduled for hysterectomy by sealed opaque envelope to 5 equal groups: Group (1) first day post hysteroscopy, Group (2) after one week, Group (3) after 2 weeks, group (4) after 3 weeks and group (5) after 4 weeks. The patients were discharged after being instructed to return immediately to the hospital should she ever develops abdominal or pelvic pain, fever or abnormal vaginal discharge.

Hysterectomy Procedure

Total abdominal hysterectomy and bilateral salpingo-oophorectomy were done without crushing the Fallopian tubes. The specimens were examined macroscopically and methylene blue dye for tubal patency was injected transcervically using a Leech Wilkinson Cannula.

Serial, at the same level, respective cuts from both tubes were put in a labeled cassette and placed in paraffin blocks. Sections were stained with hematoxylin and eosin and were examined by a histopathologist who is blinded to the side of the injected tube. The tubes were examined for any exudative reaction in the lumen, inflammation in the wall or presence of peri salpingitis. Histopathologically, the tubes were considered completely occluded if its lumen is completely filled by agglutinated plicae, partial occlusion if agglutinated plicae were seen yet part of the lumen was left patent and patent if such reactions were not seen.

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The patients' data were tabulated and analyzed using IBM® SPSS® Statistics version 23 (IBM® Corp., Armonk, NY, USA) and XLSTAT® version 2014.5.03 (Addinsoft®, Inc., Brooklyn, NY, USA). Categorical variables were presented as number and percentage and intergroup differences were compared using Fisher's exact test. P-value <0.05 was considered statistically significant.

RESULTS

In this study 43 patients were approached, eighteen of them were excluded because either of technical difficulty to achieve hysteroscopic tubal cannulation (4 cases with large endometrial polyps, 2 cases with intrauterine synechiae, 5 cases with large submucous fibroids, 4 cases with thick endometrium, 2 cases with a large endometrial cavity) or suspicion of endometrial cancer (1 case). The

age of the remaining 25 patients, ranged from 48 to 56 years (51.4 ± 2.9), with parity (3.5 ± 2.3) and body mass index (30.1 ± 8.0).



Figure1. Photograph of a Cut section of the fallopian tube with obliterated lumen (arrow) after Isoamyl-2-cyanoacrylate injection.

Table1. Indications for Hysterectomy in the five Study Groups

Indication	Group1(n=5)	Group2(n=5)	Group3(n=5)	Group4(n=5)	Group5 (n=5)	P value
Fibroiduterus	3	2	3	2	3	0.880
Adenomyosis	1	1	0	2	1	
Endometrial hyperplasia without atypia	0	2	1	0	1	
Endometrial hyperplasia with atypia	1	0	1	1	0	

Fisher's exact test (There is no statistically significant difference among the five study groups as regards the indication for hysterectomy, p-value, 0.880).

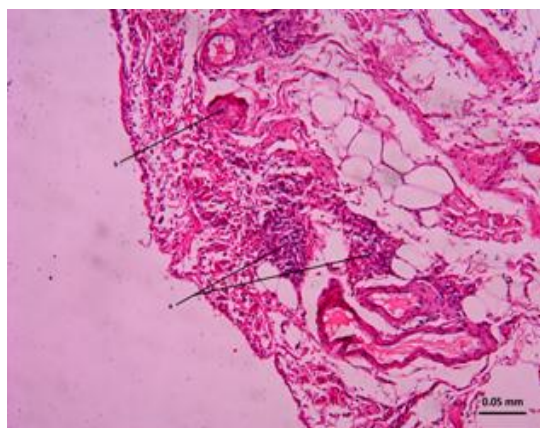


Figure2. Photomicrograph (hematoxylin and eosin stain) of mild perisalpingitis showing a. mononuclear inflammatory infiltrate and b. congestion (x40)

There was no statistically significant difference between the five groups with respect to the indications of hysterectomy (Table 1). There was mild lower abdominal pain felt in all patients at the side of the injected tube, continued for less than five minutes and does not necessitate analgesics. Twenty cases (80%) out of 25 had a negative methylene blue test

with complete obliteration of the tubal lumen on macroscopic examination of the cut sections of the injected tubes (figure1). All cases were occluded in Group 1, while group 2, 3 and 4 each had four cases (80%) and group 5 had three cases (60%) with tubal occlusion without statistically significant difference between the five groups ($p=0.871$).

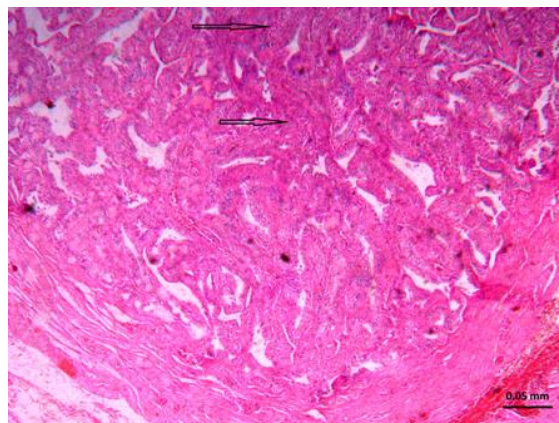


Figure3. Photomicrograph (hematoxylin and eosin stain) of cross-section of completely occluded tube with fused plicae (arrow) (x40)

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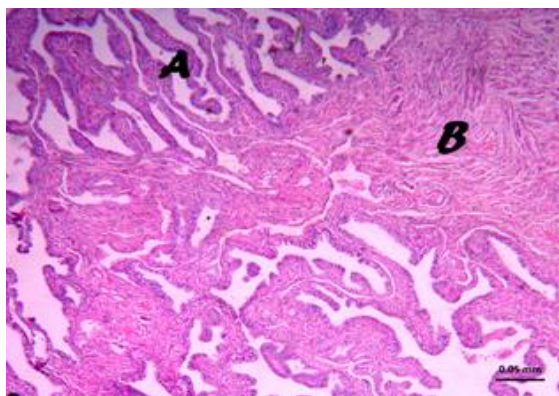


Figure4. Photomicrograph (hematoxylin and eosin stain) of cross-section of incompletely occluded tube with a. partially obliterated lumen and b. muscular distortion (x40)



Figure5. Photograph of a Hysterectomy specimen with evidence of a. Perisalpingitis and b. The gummy shaped Isoamyl-2-cyanoacrylate plug

Table2. Histopathological changes in the fallopian tube after isoamyl 2 -cyanoacrylate injection in the five Study Groups

Histopathologic examination	Group1 (n=5)	Group2 (n=5)	Group3 (n=5)	Group4 (n=5)	Group5 (n=5)	p-value
Complete tubal occlusion	3 (60%)	4 (80%)	1 (20%)	1(20%)	0	0.257
Partial tubal occlusion	1(20%)	1(20%)	3(60%)	2 (40%)	3(60%)	
No tubal occlusion	1(20%)	0	1(20%)	2(40%)	2(40%)	
Stromal tubal reaction	5	5	5	5	5	
Perisalpingitis	0	0	0	2	0	

Fisher's exact test. (There is no statistically significant difference among the five study group as regards the degree of tubal occlusion, stromal reaction, perisalpingitis, p-value, 0.257).

Histopathology of the injected tube shows tubal wall congestion with chronic nonspecific inflammation in all cases (Figure 2); while perisalpingitis was present in two cases (8%) with a fibroid uterus belong to group (4). Complete tubal occlusion was found in 9 cases (36%) (Figure 3), partial occlusion in 10 cases (40%) (Figure 4) and a patent tubal lumen in 6 cases (24%). There was one case with freely expelled

Amacryl plug in the Douglas pouch without adhesions to surrounding organs (Figure 5). There was no statistically significant difference as regards the severity of inflammatory changes or lumen occlusion of the injected tubes between the five groups (Table 2). The tubes on the control side in all cases were patent by methylene blue test and at histopathology without any degree of tubal wall inflammation.

Table3. Correlation between uterine pathology and the tubal reaction and its occlusion after Iso-amyl -2-cyanoacrylate injection

Tube histopathology and methylene blue test	Fibroid uterus (n=13)	Adenomyosis (n=5)	Endometrial hyperplasia without atypia (n=4)	Endometrial hyperplasia with atypia (n=3)	p-value
Complete tubal occlusion	5	1	2	1	0.760
Partial tubal occlusion	5	2	2	1	
No tubal occlusion	3	2	0	1	
Stromal tubal reaction	13	5	4	3	
Perisalpingitis	2	0	0	0	
Positive MB	3	1	1	0	0.851
Negative MB	10	4	3	3	

Fisher's exact test. (There is no statistically significant correlation between the uterine pathology and the result of tubal histopathology (p-value 0.760) and its occlusion (P=0.851).

Patients with fibroid uterus or Adenomyosis were having a higher failure rate for tubal occlusion, (3 out of 13 and 2 out of 5

respectively) than those with endometrial hyperplasia (one case of out of seven), without a statistically significant difference (Table 3).

DISCUSSION

In this study, single hysteroscopic tubal injection of Iso-amyl-2-cyanoacrylate, causes an immediate tubal block in 80% of cases without significant inflammatory reaction, necrosis of mucosa, or intramural fibrosis. To the best of our knowledge, there are no published data involving a study of similar methodology conducted on human beings. It is an office procedure with the use of rather cheap disposable materials and the relatively inexpensive Iso Amyl-2-cyanoacrylate (0.5 ml Amcrylate® ampoule is worth about 8\$). The only side effect is mild lower abdominal pain continued for less than five minutes after injection and no event was broken because of nuisance or irritation. Attempt to perform the procedure failed in 18 cases that were having intracavitary lesions that hindered the tubal cannulation.

The material used in this study is a cyanoacrylate derivative (CA), which were used safely and effectively in various medical indications for obstructing digestive, urinary and pulmonary fistulas^{19,20} and to ensure wounds, lacerations and corneal ulcer healing, mesh fixation for inguinal hernia²⁴ and adhesion of bone or cartilage²⁵ as well as to control bleeding from esophageal varices^{26,27}. CA converts into an inert polymer on coming in contact with moisture and solidifies rapidly within 5–10 seconds and fix in a minute²⁸. It is bacteriostatic and extremely adhesive to biological tissue which makes it beneficial in case when used to occlude hydrosalpinx prior to IVF^{29,30,31}. Higher cyanoacrylates like N-butyl-2-cyanoacrylate and iso-amyl-2-cyanoacrylate are less histotoxic with no carcinogenic effects being degraded at a slower rate than those with shorter side chain^{32,33}. The polymerization of CA is exothermic and the heat released might explain the mild pain felt by all patients immediately post injection³⁴. The metabolites of Iso-Amyl-2-Cyanoacrylate (Cyanoacetate and Formaldehyde) cause inflammation in surrounding tissues, which would help in long term tubal occlusion, besides the local anesthetic effect of the formaldehyde making the pain felt by the patient after injection being mild³⁵. For cases who were scheduled at a later date for hysterectomy (up to 4 weeks post hysteroscopy), there were no reported adverse effects from the procedure.

Histopathology of the occluded tubes in this study showed amalgamation of the plicae, mild stromal inflammation, but no serosal involvement

except in two cases which passed unnoticed clinically, one of them with Amacryl plug expelled freely in the Douglas pouch. Reviewing the hysteroscopic record of the last patient showed that there was a submucous fibroid which necessitated more maneuvering and forcing of the ureteric catheter, which probably caused more force of injecting the Isoamyl-2-cyanoacrylate and its expulsion to Douglas Pouch.

The similar effect of the n-butylacrylate on the tubal epithelium of animal model with the formation of Acrylate plug obstructing the tubal lumen without affection of the epithelium was reported³⁶. The only report involving n-butyl cyanoacrylate in humans included two cases, where radiologic guided fluoroscopic cannulation of the tubes was used to inject the CA. Follow up of these cases by hysterosalpingography for 2 years confirmed the tubal occlusion but no histopathology was done.³⁷ On the other hand, the report on the use of methyl cyanoacrylate on animal model revealed a severe tissue reaction with necrosis¹³. In human, methyl cyanoacrylate applied to Femcept device for tubal occlusion had lead to decreased amount of menstrual blood in 40% of patients possibly as a result of severe tissue reaction with endometrial damage^{38,39}. On the other hand, the use of Adiana® silicon inserts and Essure® micro inserts is associated with intense inflammation and fibrosis in the uterine tube beside the high cost of both methods and the Nickel allergy with Essure⁴⁰. Iso-amyl-2-cyanoacrylate induces immediate tubal occlusion by forming Acrylate plug and amalgamation of tubal plicae, while after Essure it needs to wait for 3 months to get complete tubal occlusion. Beside that, in women with hydrosalpinx that planning for IVF, being an inert material, will not change the internal environment of the uterine cavity and so will not adversely affect the current pregnancy should it occur. Being an office procedure and cheap, the injection could be repeated until tubal occlusion confirmed by HSG.

To test the safety and tissue effect of Iso-amyl-2-cyanoacrylate in the Fallopian tubes it should be done in patients with indications for hysterectomy, and this is only feasible in patients who were completed their families. All cases in this study were having concomitant uterine pathology so tubal cannulation and the effectiveness of the tubal occlusion would be easier if used to occlude the tubes in a healthy uterus as in cases of hydrosalpinx prior to IVF

or for sterilization. This is a rather difficult point to discuss because we do think that the degree of occlusion might be affected by the type of concomitant uterine pathology, where patients with a fibroid uterus or Adenomyosis in this study were having a higher failure rate (3 out of 13 and 2 out of 5 respectively) versus one out of seven for cases with endometrial hyperplasia.

Histopathology in this study was done primarily to assess the tissue effect of the Iso-amyl-2-cyanoacrylate and not for the tubal occlusion where methylene blue testing is the gold standard for tubal patency and the low number of occluded tubes at histopathology might have arisen from processing and distortion of the tube during sectioning. Follow up for a longer period to ensure that proper tissue reactions have occurred might increase the number of cases with complete tubal occlusion, which could not be achieved in this study, where all patients were having uterine pathology that needs treatment.

In the present days, hysteroscopy for uterine tube occlusion has been shown a low cost and less surgical interurrences than the laparoscopy, however, the main controversy is on the safety and effectiveness of the device that should be inserted in the tube^{41,42,43}. 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^{41,43}. The use of either macrolide antibiotics (erythromycin tablets) or electro coagulation was associated with high failure rate in more than 35% of cases with potentially serious complications in the later, secondary to inadvertent tubal perforation or heat transfer resulting in injury to the adjacent bowel.⁴⁴

Nowadays there are two mechanical devices, the Adiana (Adiana, Redwood City, CA) and the Essure® (Conceptus, Inc., San Carlos, CA), both of them, when inside the tube, induce the formation of granulomatous tissue and a total occlusion within three months. Currently, the Essure® is the only dispositive approved by the Food and Drug Administration (FDA) and the European Health Office (EHO)^{42, 45}. Major adverse events with the use of Essure® were reported as expulsion, perforation of the Fallopian tubes, migration of the device to the abdominal cavity and vasovagal reactions beside its high cost⁴⁶. The limitations in this study is the few number of patients and the short period of follow up and so evaluation of hysteroscopic

tubal occlusion with Iso-amyl-2-cyanoacrylate effectiveness in sterilization will require a larger sample size with a longer period of follow up.

CONCLUSION

This study demonstrates that hysteroscopic tubal occlusion with Iso-amyl-2-cyanoacrylate is safe. Being an office procedure and cheap, the injection could be repeated until complete tubal occlusion confirmed by hysterosalpingography in cases with hydrosalpinx prior to IVF.

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REFERENCES

- [1] Jack KE, Chao CR. Female voluntary contraception via minilaparotomy under local anesthesia. *Int J Gynecol Obstet.* 1992 Oct;39(2):111-6.
- [2] Bordahl PE, Raeder JC, Nordentoft J, Kirste U, Refsdal A. Laparoscopic sterilization under local or general anesthesia? A randomized study *Obstet Gynecol.* 1993 Jan;81 (1):137-41.
- [3] Bhiwandiwalla PP, Mumford SD, Feldblum PJ. A comparison of different laparoscopic sterilization occlusion techniques in 24,439 procedures. *Am J Obstet Gynecol.* 1982 Oct 1;144 (3):319-31.
- [4] Camus E, Poncelet C, Goffinet F et al. Pregnancy rates after in-vitro fertilization in cases of tubal infertility with and without hydrosalpinx: a meta-analysis of published comparative studies. *Hum Reprod.* 1999 May;14 (5):1243-9.
- [5] Vandromme J, Chasse E, Lejeune B, Van Rysselberge M, Delvigne A, Leroy F. Hydrosalpinges in in-vitro fertilization: an unfavourable prognostic feature. *Hum Reprod.* 1995 Mar;10(3):576-9
- [6] Johnson NP, Mak W, Sowter MC. Surgical treatment for tubal disease in women due to undergo in vitro fertilisation.. *Cochrane Database Syst Rev.* 2004; (3):CD002125. Review. Update in: *Cochrane Database Syst Rev.* 2010; (1):CD002125.
- [7] Gelbaya TA, Luciano GN, Fitzgerald CT, Horne G, Brison DR, Lieberman BA. Ovarian response to gonadotropins after laparoscopic salpingectomy or the division of fallopian tubes for

- hydrosalpinges. *Fertil Steril*. 2006 May; 85 (5) :1464-8. Epub 2006 Apr 3.
- [8] Surrey ES, Schoolcraft WB. Laparoscopic management of hydrosalpinges before in vitro fertilization-embryo transfer: salpingectomy versus proximal tubal occlusion. *Fertil Steril*. 2001 Mar;75(3):612-7.
- [9] Schmitz-Rode T, Ross PL, Timmermans H, Thurmond AS, Günther RW, Rösch J. Experimental nonsurgical female sterilization: transcervical implantation of microspindles in fallopian tubes. *J Vasc Interv Radiol*. 1994 Nov-Dec;5(6):905-10.
- [10] Erb RA, Reed TP. Hysteroscopic oviductal blocking with formed-in-place silicone rubber plugs. *J Reprod Med*. 1979 Aug;23(2):65-8.
- [11] Maubon AJ, Thurmond AS, Laurent A, et al. Tubal sterilization by means of selective catheterization: comparison of a hydrogel and a collagen glue. *J Vasc Interv Radiol*. 1996 Sep-Oct;7(5):733-6.
- [12] Zipper J, Cole LP, Goldsmith A, Wheeler R, Rivera M. Quinacrine hydrochloride pellets: preliminary data on a nonsurgical method of female sterilization. *Int J Gynecol Obstet*. 1980;18(4):275-9.
- [13] Berkey GS, Nelson R, Zuckerman AM, Dillehay D, Cope C. Sterilization with methyl cyanoacrylate-induced fallopian tube occlusion from a nonsurgical transvaginal approach in rabbits. *J Vasc Interv Radiol*. 1995 Sep-Oct;6(5):669-74.
- [14] Na ED, Cha DH, Cho JH, Kim MK. Comparison of IVF-ET outcomes in patients with hydrosalpinx pretreated with either sclerotherapy or laparoscopic salpingectomy. *Clin Exp Reprod Med*. 2012 Dec;39(4):182-6. doi: 10.5653 / cerm.2012.39.4.182
- [15] Zhang WX, Jiang H, Wang XM, Wang L. Pregnancy and perinatal outcomes of interventional ultrasound sclerotherapy with 98% ethanol on women with hydrosalpinx before in vitro fertilization and embryo transfer. *Am J Obstet Gynecol*. 2014 Mar;210(3):250.e1-5.
- [16] Rivoire HC, Fagundes DJ, Bigolin S, Fagundes AT. Hysteroscopy and the butyl-cyanoacrylate on experimental sterilization of rabbit uterine tubes. *Acta Cir Bras*. 2007 Sep-Oct;22(5):396-400.
- [17] Poza Cordon J, Froilan Torres C, Burgos García A, Gea Rodriguez F, Suárez de Parga JM. Endoscopic management of esophageal varices. *World J Gastrointest Endosc*. 2012; Jul 16; 4(7): 312–322.
- [18] Abd Elrazek AE, Yoko N, Hiroki M, et al. Endoscopic management of Dieulafoy's lesion using Isoamyl-2-cyanoacrylate. *World J Gastrointest Endosc*. 2013 Aug 16;5(8):417-9.
- [19] Cagirici U, Cetin Y, Cakan A, Samancilar O, Veral A, Askar FZ. Experimental use of N-butyl cyanoacrylate tissue adhesive on lung parenchyma after pulmonary resection. *Thorac Cardiovasc Surg*. 2007 Apr;55(3):180-1.
- [20] Muto G, D'Urso L, Castelli E, Formiconi A, Bardari F. Cyanoacrylic glue: a minimally invasive nonsurgical first line approach for the treatment of some urinary fistulas. *J Urol*. 2005 Dec;174(6):2239-43.
- [21] Rosenfield RB, Stones RE, Coates A, Matteri RK, Hesla JS. Proximal occlusion of hydrosalpinx by hysteroscopic placement of microinsert before in vitro fertilization-embryo transfer. *Fertil Steril*. 2005 May;83(5):1547-50.
- [22] Darwish AM, El Saman AM. Is there a role for hysteroscopic tubal occlusion of functionless hydrosalpinges prior to IVF/ICSI in modern practice? *Acta Obstet Gynecol Scand*. 2007;86(12):1484-9
- [23] Causton BE (1992) Medical and dental adhesives. In: *Materials science and technology: a comprehensive treatment*. eds. by Cahn RW, Haasen P, Kramer EJ. *Medical and Dental Materials Vol. 14*, 291–2, VCH Publishers Inc., New York
- [24] Jourdan IC, Bailey ME. Initial experience with the use of n-butyl-2-cyanoacrylate glue for the fixation of polypropylene mesh in laparoscopic hernia repair. *Surg Laparosc endosc*. 1998 Aug; 8(4): 291-93.
- [25] Kim Y. Use of cyanoacrylate in fascial bone fracture. *J craniofac surg*. 1997 May;8(3):229-34.
- [26] Zheng F, Lin X, Tao L. A randomized trial of endoscopic treatment of acute gastric variceal hemorrhage: n-butyl-2- cyanoacrylate injection versus band ligation. *J Gastroenterol Hepatol*. 2012;27 (S5):113.
- [27] Qiao W, Ren Y, Bai Y, Liu S, Zhang Q, Zhi F. Cyanoacrylate Injection Versus Band Ligation in the Endoscopic Management of Acute Gastric Variceal Bleeding: Meta-Analysis of Randomized, Controlled Studies Based on the PRISMA Statement. *Medicine*. 2015 Oct; 94(41):e1725.
- [28] Maartenese. S, Beleman W.A., Dunker M.S., et al. Randomized study of the effectiveness of closing laparoscopic trocar wounds with octylcyanoacrylate, adhesive papertape or poliglecaprone. *British Journal of Surgery*. 2002 Nov;89(11):1370-5.
- [29] Devrukhkar VN, Hegde RJ, Khare SS, Saraf TA. Evaluation of isoamyl 2-cyanoacrylate tissue adhesive in management of pediatric lacerations: An alternative to suturing. *Ann Maxillofac Surg*. 2015 Jan-Jun;5(1):49-54.

- [30] Eiferman RA, Snyder JW. Antibacterial effect of cyanoacrylate glue. *Arch Ophthalmol.* 1983 Jun;101(6):958-60.
- [31] Jandinski J, Sonis S. In vitro effects of isobutyl cyanoacrylate on four types of bacteria. *J Dent Res.* 1971 Nov-Dec;50(6):1557-8.
- [32] Samuel PR, Roberts AC, Nigam A. The use of Indermil (n-butyl cyanoacrylate) in otorhinolaryngology and head and neck surgery. A preliminary report on the first 33 patients. *J Laryngol Otol.* 1997 Jun;111(6):536-40.
- [33] Nagpal BM, Kumar G, Nagi GS, Singh P. Sutureless closure of operative skin wounds. *Med J Armed Forces India.* 2004 Apr;60(2):131-3.
- [34] Coover HW, Joyner FB, Sheare TH, et al. Chemistry and performance of cyanoacrylate adhesives. *Soc Plastic Engrs. J.* May 1959;15:413.
- [35] Edmonson MB. Foreign body reactions to dermabond. *Am J Emerg Med.* 2001 May;19(3):240-1.
- [36] Bigolin S, Fagundes DJ, Rivoire CH, Fagundes AT, Fagundes AL. Transcervical hysteroscopic sterilization using cyanoacrylate: A long-term experimental study on sheep. *J Obstet Gynaecol Res.* 2009 Dec;35(6):1012-8.
- [37] Pelage JP, Herbreteau D, Paillon JF, Murray JM, Rymer R. Selective salpingography and fallopian tubal occlusion with n-butyl-2-cyanoacrylate: report of two cases. *Radiology.* 1998 Jun;207(3):809-12
- [38] Stevenson, TC and Taylor DS. The effect of methyl Cyanoacrylate on human fallopian tube and endometrium. *J Obstet.Gynecol.* 79: 1028, 1972
- [39] GUZMAN-SERANI R, ROSA G. and COLE L. P. Evaluation of two applications of methyl cyanoacrylate for female sterilization. *Adv. Contracept.* 2 (1986) 91-95
- [40] Basinski CM. A Review of Clinical Data for Currently Approved Hysteroscopic Sterilization Procedures *Rev Obstet Gynecol.* 2010 Summer; 3(3): 101–110
- [41] Cooper JMJ, Carignan CS, Cher D, Kerin JF. Microinsert nonincisional hysteroscopic sterilization. *Obstet Gynecol.* 2003 Jul;102(1):59-67.
- [42] Ubeda A, Labastida R, Dexeus S. Essure: a new device for hysteroscopic tubal sterilization in an outpatient setting. *Fertil Steril.* 2004 Jul;82(1):196-9.
- [43] Levie MD, Chudnoff SG. Office hysteroscopic sterilization compared with laparoscopic sterilization: a critical cost analysis. *J Minim Inv Gynecol.* 2005 Jul-Aug;12(4):318-22.
- [44] Beerthuizen R. State-of-the-art of non-hormonal methods of contraception: V. Female sterilisation. *Eur J Contracept Reprod Health Care.* 2010 Apr;15(2):124-35.
- [45] Hastings-Tolsma M, Nodine P, Teal SB. Essure: hysteroscopic sterilization. *J Midwifery Women Health.* 2006 Nov-Dec;51(6):510-4.
- [46] Edmonton AB: *Hysteroscopic tubal sterilization.* Institute of Health Economics. 2014