

Original article

HYDROSALPINX AND DISTRIBUTION OF PREGNANCIES AMONG LAPAROSCOPICALLY TREATED PATIENTS

ХИДРОСАЛПИНКСОТ ВО КОРЕЛАЦИЈА СО СТАПКАТА НА БРЕМЕНОСТИ КАЈ ЛАПАРОСКОПСКИ ТРЕТИРАНИТЕ ПАЦИЕНТКИ

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Abstract

Introduction. Hydrosalpinx is a common medical condition encountered among female population with infertility issues. One or both fallopian tubes can be filled with a substantial amount of fluid, making them dilated and dysfunctional, usually as a result of an injury or infection. Damages of different degrees can be seen on the mucosal lining, which compromise the processes of normal fertilization and zygote passage.

Methods. We retrospectively analyzed clinical records from a period of five years (2013-2017), selecting patients diagnosed as having unilateral or bilateral hydrosalpinx. Clinical files were divided by years and according to the treatment protocol used. Our scope of interest was focused on patients who were treated surgically, with different types of laparoscopic interventions. A total of 74 patients met our criteria for selection.

Results. Two groups were related to conservative laparoscopic approaches and one to complete radical surgical treatment, unilateral or bilateral salpingectomy. Patients in the first group, 9(16.36%), were treated with a laparoscopically-guided creation of salpingostomy. The second group comprised patients treated only with bilateral chromopertubation and consisted of 17 (30.91%) patients. The third, and the most numerous group comprised 29(52.7%) patients treated with salpingectomy. Bilateral salpingectomy was performed in 9(31.03%) and unilateral in 20(68.97%) patients, showing that majority of patients were treated with unilateral salpingectomy, after intraoperative evaluation of tubal patency of the contralateral uterine tube.

A total number of 30 patients (54.5%) had successful pregnancies, which ended up with a desired outcome, healthy live birth. Procedures for artificial reproduction and successful pregnancies achieved with IVF were recorded in 11(36.67%) patients and in the remaining

19(63.33%) patients pregnancies were achieved via spontaneous conception.

Conclusion. Hydrosalpinx management is mainly influenced by the local tubal changes evaluated laparoscopically and can be surgically treated, either conservative or radical. Conservative approaches lead to fair chances of spontaneous conception and successful pregnancies. An integrated management of hydrosalpinx with bilateral salpingectomy and postsurgical usage of artificial reproduction techniques also leads to a substantial cumulative pregnancy rate.

Keywords: hydrosalpinx, surgical approach, pregnancy rates

Апстракт

Вовед. Хидросалпинксот е многу честа дијагноза во клиничката гинеколошка пракса, особено кај пациентките со проблеми поврзани со инфертилитет. Едната или обете Фалопиеви туби може да се исполнат со значителна количина на течност, што доведува до нивна дилатација и ги прави нефункционални, обично како резултат на повреда на ткивото или инфекција. Оштетувања со различен степен може да се видат долж мукозата и тие доведуваат до нарушување на процесите на нормална фертилизација и транспорт на зиготот.

Методи. Направена е ретроспективна студија на клинички материјал од период од 5 години (2013-2017 година), притоа селектирајќи пациентки кои биле оперативно третирани, под дијагноза за унилатерален или билатерален хидросалпинс. Податоците потоа се поделени по години, според типот на третман кој бил употребен кај пациентките. Нашата цел беше да се детектираат пациентките кои биле третирани хируршки со различни типови на лапароскопски интервенции. Вкупен број од 74 пациентки влегоа во студијата, задоволувајќи ги сите критериуми.

Резултати. Во групата на пациентки третирани со лапароскопски конзервативен пристап, со презервација на тубите, зависно од типот на третман пациентките ги поделивме до две подгрупи. Дополнително се креираше трета група во која се опишани пациентки третирани со лапароскопски дефинитивен третман, унилатерална или билатерална салпингектомија. Во првата група, 9(16.36%) се спаѓаат пациентки кои се третирани лапароскопски, со формација на салпингостома (тубостома). Втората група на пациентки се третирани со билатерална хромопертубација, 17(30.91%). Третата, а притоа и најголема група на пациентки, се состои од 29 (52.7%) пациентки, од кои билатерална салпингектомија била изведена кај 9(31.03%), додека пак унилатерална била направена кај 20 (68.97%). Јасно е од резултатите најголем дел од пациентките биле третирани со унилатерална салпингектомија, секако по интраоперативна потврда за комплетна проодност на контралатералната утерина туба. Кај вкупен број од 30 пациентки (54.5%) биле забележани успешни бремености кои завршиле со раѓање на живородени деца. Од тој вкупен број на пациентки кои оствариле бременост кај 11 пациентки (36.67%) биле употребени некоја од процедурите за артефициелна репродукција и биле постигнати успешни бремености. Кај останатиот број на пациентки 19(63.33%) остварена била спонтанa концепција.

Заклучок. Третманот на хидросалпинкс, како честа состојба кај пациентките што се борат со инфертилитет, главно зависи од степенот на локални тубарни промени, кои истовремено можат да бидат и евалуирани и третирани лапароскопски. Конзервативниот хируршки пристап доведува до задоволителна можност за спонтанa концепција и остварување на успешна бременост. Модерниот интегриран хируршки пристап подразбира пак билатерална салпингектомија и постоперативна употреба на некоја од техниките за артефициелна репродукција, пристап што исто така води до задоволителна кумулативна стапка на успешни бремености.

Клучни зборови: хидросалпинкс, хируршки пристап, стапка на бремености

Introduction

Hydrosalpinx is a common medical condition encountered among female population with infertility issues. One or both fallopian tubes can be filled with a substantial amount of fluid, making them dilated and dysfunctional, usually as a result of an injury or infection. Often the affected area can become substantially swollen and grow to even as big as few centimeters in diameter. Damages of different degrees can be seen on the mucosal lining, which compromise the processes of

normal fertilization and zygote passage. The pathophysiology of this condition is unique, usually related to pelvic inflammatory disease or excessive tissue buildup due to endometriosis. Inflammation results in destruction of the mucosal lining and fimbria, fusing them together until complete distal obstruction of the tubes. Hydrosalpinges can be divided in three groups, hydrosalpinx simplex, follicularis and sactosalpinx, depending on the anatomical changes. Destruction of the tubal epithelium leads to loss of membrane polarity, expression of membrane transporters, reabsorption and release of a large amount of inflammatory mediators and increase of serosa to mucosa fluid flow [1].

Some cases of hydrosalpinx can be easily repaired with the surgical procedure of neosalpingostomy or tubostomy, which allows pregnancy to occur naturally. Recovery from this procedure is relatively rapid and tubal function is completely resumed within a few days. Pregnancy rates following surgical tubal reconstruction are 10% in the year following neosalpingostomy. Due to this fact and also facing with the increased risk of ectopic pregnancies in these patients most women with hydrosalpinx and extensive tubal damages are advised to move directly to salpingectomy and in vitro fertilization (IVF). Major debates have been conducted upon the impaired IVF outcome in patients with hydrosalpinx, mainly focused on the embryotoxic properties of the fluid, distorted endometrial receptivity and low percentage of successful implantations [2].

Tubal factors responsible for infertility issues account for an approximately 25% of the cases, whereas the most severe manifestation is hydrosalpinx. 10-30% of all tubal diseases can be described as unilateral or bilateral hydrosalpinges, with variable degrees of tubal distension or dilatation and presence of distal tubal occlusion. Mainly these patients present with mild lower abdominal pain and concerns related to infertility problems [3]. Surgical interventions, both conservative and definitive, are very successful and thought to improve the chances of fertilization, zygote transport, implantation and pregnancies in the future. The majority of pregnancies occur during the first year postoperatively [4]. Diagnostic evaluation and decision on how to treat tubal diseases, especially hydrosalpinx, can be very difficult. It comprises of many surgical, medical, social, emotional and economic factors [5]. Unilateral or bilateral salpingectomy has been one of the most frequently employed surgical interventions during the past years, mainly due to the theories for the possible effect of hydrosalpinx fluid on the human embryos. The majority of poor IVF results have been tracked in the group of patients with hydrosalpinx, compared to women with other tubal factor-related infertility [6]. Hydrosalpinges are mainly related to *Chlamydia trachomatis* infection, which is the main cause for pelvic inflammatory disease and 30% of these patients undergoing IVF have unilateral or bilateral hydrosalpinx present [7]. Labo-

ratory investigations were conducted in order to find the correlation between hydrosalpinges and reduced pregnancy rates in this population of patients. Changes as impaired ovarian function, endometrial damage, dilutional effect on essential nutrients and substrates, direct cytotoxic effect on gametes and embryos, inflammatory responses, mechanical washout of embryos, effect on endometrial receptivity and implantation rates were recorded and directly correlated with undesired outcomes [8-12]. The aim of this study was to find the correlation between different approaches in the surgical treatment of hydrosalpinx and post-treatment pregnancy rates.

Material and methods

We retrospectively analyzed clinical records from a period of five years (2013-2017), selecting patients diagnosed as having unilateral or bilateral hydrosalpinx. Clinical files were divided by years and according to the treatment protocol used. Our scope of interest was focused on patients who were treated surgically, with different types of laparoscopic interventions. A total of 74 patients met our criteria for selection. Inclusion criteria that we used during records' assortment were complete data about duration of infertility, microbiological analyses and status, complete data about diagnostic procedures, treatment protocol selection, surgical protocol and detailed information related to postoperative period. All patients were contacted and data related to pregnancy rates were collected. Due to a lack of complete and detailed information 19 patients were excluded from the study, making the final group comprising of 55 patients. All patients were evaluated at the University Clinic for Obstetrics and Gynecology, where they went through a standardized diagnostic protocol for hydrosalpinx. From the collected clinical records we collected data related to ultrasound exams, hysterosalpingogram, past and present microbiological status, presence of additional gynecological conditions, reproductive history and surgical treatment employed. After a proper preoperative preparation a total number of 55 patients was surgically treated at our surgical unit, using a KARL STORZ laparoscope. Additionally, they were divided in two groups comprising patients treated with more conservative surgical methods and those treated with radical surgical treatment, unilateral or bilateral salpingectomy. Patients were directly contacted and asked about their postoperative period. They provided us with data related to achieved conceptions, either spontaneous or via methods for artificial reproduction and number of successful pregnancies.

Results

The final group of analyzed clinical records and patients being directly contacted consisted of 55 patients. We analyzed a period of five years (2013-2017) and

divided the patients according to the year of surgical treatment of hydrosalpinx. Yearly distribution of patients showed that 8 (14.55%) were treated during 2013, 10 (18.18%) during 2014, 18(32.73%) during 2015, 7(12.73%) during 2016 and 12(21.81%) during 2017. Minimal age recorded was 21 years and maximal age was 46 years (interval 33±12, average age 33.09). Analysis of admission diagnosis showed that 17 (30.9%) patients were admitted as having bilateral salpingeal involvement and 38(69.1%) as having unilateral involvement.

Hysterosalpingography (HSG) scans revealed information upon tubal anatomy distortion and tubal patency. All 55 patients were with HSG results for hydrosalpinx, which in 23(41.8%) patients was described as bilateral and in 32(58.2%) patients as unilateral. During analysis of HSG results we recorded additional gynecological conditions, described as septum uteri and peritubal adhesions. A total number of 20 (36.3%) patients had septum of different degree and they received additional treatment, hysteroscopic resection of septum, while 9(16.36%) patients had an additional HSG changes explained as peritubal adhesions.

Data related to reproductive history were extracted from the collected clinical records. We analyzed all pregnancies reported, abortions, ectopic pregnancies and successful pregnancies, which resulted in a live birth. The analysis of these data showed that 45(81.8%) patients were nulliparous and 10(18.2%) patients were parous. In the second group all patients reported one or more live births. All patients had a complete documentation about their past microbiological status and 21 (38.2%) patients had a previous history of *Chlamydia trachomatis* infection.

All clinical records were analyzed in details regarding data related to infertility status. Patients had been asked to give information about infertility problems, duration of infertility and treatments used in the past. Minimal duration of infertility, after which patients asked for evaluation and treatment, was one year and maximal duration was 20 years (average years of infertility 6.4 years). Surgical protocols of laparoscopic treatment were extracted from clinical records and based on that data patients were divided in three groups. Two groups were related to conservative laparoscopic approaches and one to complete radical surgical treatment, unilateral or bilateral salpingectomy. Patients in the first group, 9 (16.36%), were treated with a laparoscopically guided creation of salpingostomy. The second group comprised patients treated only with bilateral chromopertubation and consisted of 17(30.91%) patients. The third, and the most numerous group consisted of 29(52.7%) patients treated with salpingectomy. Bilateral salpingectomy was performed in 9(31.03%) and unilateral in 20(68.97%) patients, showing that majority of patients were treated with unilateral salpingectomy, after intraoperative evaluation of tubal patency of the contralateral uterine tube.

Data collected from the postoperative period, with a mean follow-up of 15 months, provided us with information related to additional infertility treatment and conceptions achieved. A total number of 30 patients (54.5%) had successful pregnancies, which ended up with a desired outcome, healthy live birth. Procedures for artificial reproduction and successful pregnancies

achieved with IVF were recorded in 11 (36.67%) patients and in the remaining 19 (63.33%) patients pregnancies were achieved via spontaneous conception (Table 1). Methods of delivery were also analyzed and the distribution of spontaneous deliveries and cesarean sections was equal (15 patients, 50% in both groups).

Table 1. Distribution of pregnancies among patients in correlation with methods of treatment

Treatment	Number of pregnancies
Chromopertubation	9, from which 7 spontaneous and 2 ART
Creation of tubostoma	6, from which 4 spontaneous and 2 ART
Unilateral salpingectomy	9, from which 8 spontaneous and 1 ART
Bilateral salpingectomy	6, all ART

Our special field of interest was the group of patients in which the laparoscopic chromopertubation probe showed that one tube was overall healthy and patent, while contralateral was distorted, pathologically changed and obstructed. This group consisted of 20 patients, who were surgically treated with unilateral salpingectomy.

From the total number of successful pregnancies achieved (30), nine were recorded in this group. Interestingly, pregnancies among these patients were mainly spontaneous conceptions, with only one pregnancy achieved via IVF (Figures 1, 2 and 3).

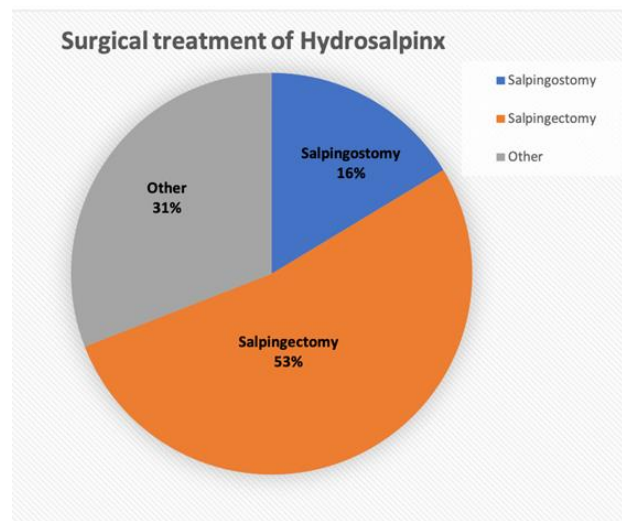


Fig. 1. Distribution of different surgical treatment options in patients with hydrosalpinx

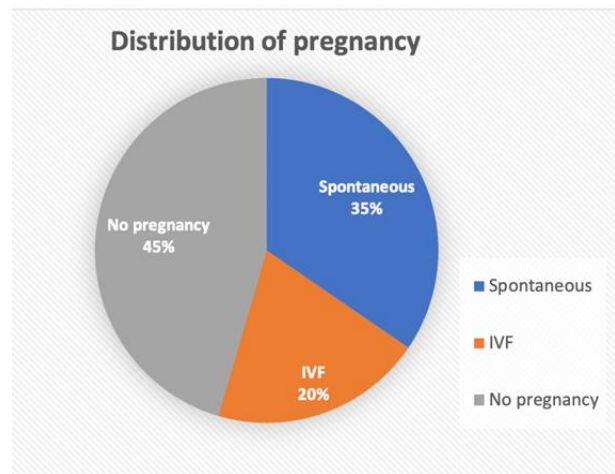


Fig. 2. Pregnancy rates in treated patients

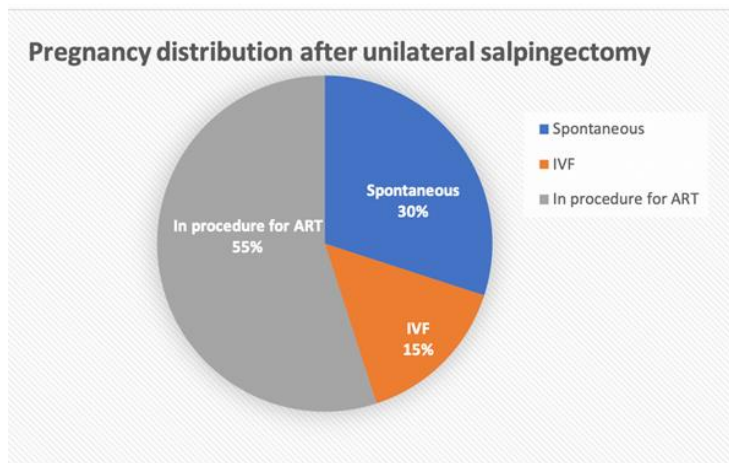


Fig. 3. Distribution of pregnancies in the group of patients treated with unilateral salpingectomy

Discussion

Increasing rates of gynecological infections and incidence of pelvic inflammatory diseases among young fertile population lead to a considerable rise in patients diagnosed with hydrosalpinx. This condition is mainly recorded among infertile young female population. Many debates and researches have been conducted during the past decade in order to detect and explain factors of hydrosalpinx that influence conception rates. Also, hydrosalpinges have been related to IVF success rates. Several studies showed that presence of hydrosalpinx can reduce the probability of achieving a pregnancy by 50% and at the same time double the rate of spontaneous abortions [13]. Hydrosalpinx fluid is the main reason for lower pregnancy rates in these patients. Any surgical intervention that interfere the communication between uterus and tube would remove the leakage of hydrosalpinx fluid and restore pregnancy rates particularly seen in patients treated with salpingectomy. Many studies which were conducted during the past ten years showed that hydrosalpinx fluid had major embryotoxic properties, which was proved *in vitro* on human embryos. Undiluted hydrosalpinx fluid resulted in a 50% reduction in blastocyst development compared with control medium. Mainly patients did not exhibit presence of pathogenic microorganisms at the time of evaluation, but slightly elevated concentrations of endotoxins have been demonstrated in individual fluids as a sign of previous *Chlamydia trachomatis* infection. For these patients there is still a debate with regard to the effectiveness of aspiration of hydrosalpingeal fluid before initiation of IVF protocol [14]. Oxidative stress, which is defined as an elevated concentration of reactive oxygen species on cellular level, has been employed in the function of various reproductive conditions, such as hydrosalpinx, proposing that these products can change the environment for fertilization and decline its success [15]. Hydrosalpin-

geal fluid has been related to improper embryo development, due to low energy substrate distribution, mainly related to glucose and pyruvate transport. Glucose concentration is generally found to be very low in hydrosalpinx fluid, compared to levels in normal tubal fluid. Lack of nutrients leads to impaired development of blastocysts and impaired implantation capacity of the embryo [16-18]. A substantial number of studies have evaluated the impact of hydrosalpingeal fluid on endometrial receptivity, due to a high concentration of cytokines. Some of them focused on the role of fluid leakage through the uterine cavity, causing simple embryo disposal, or wash out [19-21].

Tubal diseases have been reported to be responsible for 20-25% of infertility issues and the main discussion is focused on how to treat them, especially hydrosalpinges. Many studies increased the awareness of tubal factors for infertility and pointed out the main protocols for diagnosis and treatment of hydrosalpinx. One review compared tubal surgery, spontaneous conception, tubal surgery and IVF. The first line treatment offered for women aged less than 35 years, especially in those with unilateral tubal pathology, should be tubal surgery. IVF should be offered to patients older than 35, with additional factors responsible for the couples' infertility, if severe tubal disease is present or if there has been more than 12 months post-surgery without successful conception. Many authors evaluated the outcome of pregnancies in patients with hydrosalpinx treated with minimally invasive alternative therapies, due to the dense pelvic adhesions. They compared laparoscopic treatments such as salpingectomy, tubal occlusion, hysteroscopic insertion of devices for tubal occlusion and aspiration of hydrosalpingeal fluid and concluded that laparoscopic surgical treatment should be considered in all patients diagnosed with hydrosalpinx, especially in those preparing for IVF [22].

Analyzing the results of natural conception rate after treatment of hydrosalpinx with laparoscopic salpingecto-

my showed that clinical pregnancy rate was 27%, in the hands of experienced surgeons who most often publish their results. During the past years, due to the high successful rates and advent of assisted conception treatment, tubal surgery is not commonly offered to women with hydrosalpinges, which has been counter-productive because there is a detected rise in the number of natural conceptions following surgical laparoscopic treatment of hydrosalpinx. One systematic review and meta-analysis of 22 observational studies revealed that the cumulative pregnancy rate after laparoscopic salpingostomy was 8.7% at 6 months, 13.3% at 9 months, 20% at 12 months, 21.2% at 18 months and 25.5% at 24 months post-surgery. The findings of this systematic review suggest that salpingostomy can be an effective alternative treatment strategy in patients with hydrosalpinx which are poor candidates for salpingectomy, due to dense per tubal adhesions [23].

Eighty-one patients, who were infertile and diagnosed with uni- or bilateral hydrosalpinx, were planned for surgical treatment, during a period of five years. During laparoscopy a systematic evaluation of the tubes was firstly conducted and the local management protocol was based on validated tubal prognostic values. Surgery was conservative, neosalpingostomy, or radical, salpingectomy. Neosalpingostomy was performed in 35 patients and salpingectomy in 46 patients. The overall cumulative pregnancy rate was 61% for couples who completed the treatment. Among patients with at least one functional tube, the overall cumulative pregnancy rate was 63.3%, with a spontaneous pregnancy rate of 30.4% [24].

Hydrosalpinx has been tracked as a major problem related to tubal factors of infertility and its treatment is of a great importance. Some studies compared different approaches such as salpingectomy, tubal occlusion and neosalpingostomy, with an accent on the cumulative pregnancy rates post-surgery. Additional analyses were conducted to point out the impact of different treatment protocols on IVF. Almost similar responses to controlled ovarian stimulation and pregnancy outcomes were observed in patients treated with salpingectomy, tubal occlusion and neosalpingostomy [25].

In patients with tubal obstruction, but intact endothelium morphology, we can choose the creation of a tubostoma as the most appropriate treatment with substantial success in achieving spontaneous implantation (in our study 66.6% among pregnant patients).

Presence of hydrosalpinx undoubtedly impairs the outcome of IVF treatment. It can be improved by simple removal of the tube, but some concerns rose regarding its feasibility and safety. One meta-analysis evaluated the efficiency of hydrosalpinx aspiration with or without sclerotherapy, compared with salpingectomy and compared to no treatment. Authors were mainly focused on recurrence rate, fertility outcomes and adverse events. The overall recurrence rates of hydrosalpinx after

aspiration with or without sclerotherapy were 21.7% to 30.5% and 21.8% to 32.5%, respectively. Clinical pregnancy rates were similar between group treated with salpingectomy and those treated with aspiration and sclerotherapy. Compared to no intervention, treatment with tubal aspiration led to a significant increase in the clinical pregnancy rates. In selected cases aspiration and sclerotherapy can be used as an alternative to salpingectomy [26]. Recent studies have raised awareness about the effect of salpingectomy on ovarian function. Salpingectomy, as the most aggressive form of tubal surgery, may be performed for various tubal diseases, including hydrosalpinx, as a method to enhance the fertility. Although salpingectomy has an overall positive effect on the spontaneous conception rates (when it is unilateral) and the successful outcomes with IVF treatment (when it is bilateral) meta-analysis showed that it was not statistically related to the ovarian function. Various authors have stated that in limited cases salpingectomy was related to an unaware removal of a functional ovarian tissue, leading to a reduction of the ovarian function. There are conflicting studies that show some slight impairment in the parameters of ovarian function and reserve, but they are mainly in patients who underwent salpingectomy for an ectopic pregnancy. This field of research is still wide and opened for conducting of new studies [27].

To test the hypothesis that IVF pregnancy rates for patients with tubal factor infertility were improved after surgical treatment, a group of authors retrospectively evaluated IVF program success in patients treated in a private infertility clinic. A total of 160 patients undergoing 238 cycles of IVF were evaluated and surgical intervention improved implantation and pregnancy rates in patients with more than one prior failed cycles (16.1% and 37.5%). The type of selected surgery did not affect success rates in this study [28].

Some authors suggest that surgical treatment should be considered for all women with hydrosalpinges prior to IVF treatment. Previous protocols supported only unilateral salpingectomy for unilateral hydrosalpinx and bilateral salpingectomy for bilateral hydrosalpinx. Recent reviews of literature provide evidence that laparoscopic tubal occlusion provides equal rates of success [29]. Ovarian response in patients with hydrosalpinx undergoing IVF treatment was also evaluated. One study evaluated patients aged <37 years, undergoing IVF 12 months post-surgery. Differences found among these patients showed that pregnancy rate was not only influenced by the type of surgery employed but also by the factors such as clinical status, selection of stimulation protocol and total number of oocytes retrieved [30].

When we face cases with destroyed tubal endothelium morphology, tubal obstruction and hydrosalpinx, but at the same time the contralateral ovarian tube is morphologically normal, we can choose laparoscopic unilateral salpingectomy as a choice of successful treatment.

With this approach we can reach appreciable percentage of cases with spontaneous pregnancies (89% in our study, which means eight of nine patients achieved spontaneous implantation).

A study for evaluation of differences in uterine and ovarian blood flows prior and after surgery for hydrosalpinx was conducted. In a university teaching hospital 60 patients were treated surgically and parameters as uterine and ovarian artery pulsatility index, resistance index, flow index, vascularization flow index, 3D Doppler vascularization index, endometrial and ovarian volume were recorded. They concluded that hydrosalpinx was majorly correlated with impaired endometrial and ovarian blood flows, which in return may adversely affect endometrial receptivity and oocyte quality [31].

Conclusion

Hydrosalpinx management is mainly influenced by the local tubal changes evaluated laparoscopically and can be surgically treated, either conservative or radical. Conservative approaches lead to fair chances of spontaneous conception and successful pregnancies. An integrated management of hydrosalpinx with bilateral salpingectomy and post-surgical usage of artificial reproduction techniques also leads to a substantial cumulative pregnancy rate.

Conflict of interest statement. None declared.

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