

Efficacy and Safety Analysis of Modified HSG for Infertile Patients

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Objective: To test the efficacy and safety of modified hysterosalpingography (HSG) for infertile patients. Altogether 110 infertile cases from March 2018 to July 2020 were grouped into the observation group (OG, 58 cases) and the control group (CG, 52 cases) according to different therapies. The OG was treated with modified HSG, while the CG was treated with conventional HSG. The tubal patency after treatment, sex hormone levels before and after therapy [including luteinizing hormone (LH), follicle stimulating hormone (FSH), estradiol (E2)], changes in uterine volume and endometrial thickness before and after therapy were tested and compared between the CG and the OG. The individuals were followed up for one year, and the pregnancy success rate was recorded. Finally, the adverse reactions of the CG and the OG after treatment were recorded and compared. After treatment, the sex hormone level, tubal patency, uterine volume and endometrial thickness of the CG and the OG were markedly elevated, but the improvement of the OG was more obvious than that of the CG. Follow-up analysis revealed that the pregnancy success rate of the OG was markedly higher than that of the CG, and the incidence of adverse reactions in OG was markedly lower than that in CG. The modified HSG can effectively improve the pregnancy situation of patients and has higher safety compared with the traditional HSG, so it is worth popularizing in clinic.

Keywords: infertility, improved HSG, curative effect, safety

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INTRODUCTION

Infertility refers to those who have a normal sexual life after marriage and have not been pregnant for one year without taking contraceptive measures, and it is a common gynecological disease in clinic¹. In recent years, due to the change of social environment and the increase of pressure in female, the risk of infertility among women has increased markedly, which poses a serious threat to reproductive health of women². The fallopian tube is the place where sperm and egg meet, and the key way to transport fertilized eggs, so the smoothness of fallopian tube will directly affect the fertility of women^{3,4}. However, most infertile patients usually show obvious symptoms such as tubal obstruction and pathological changes,

which may be caused by bacterial or mycoplasma infection of the fallopian tubes, which further leads to hydrosalpinx or obstruction of the fallopian tubes, and finally affects the structure and function of the fallopian tubes^{5,6}.

Hysterosalpingography (HSG) is an important examination method to understand the condition of uterus and fallopian tubes. HSG can not only check the causes and location of fallopian tube diseases, but also has a good therapeutic effect⁷. And HSG has been widely used in clinic for its high sensitivity and low false negative rate, but it also has some shortcomings, for example, for patients with abnormal uterine position, HSG can't show the shape of uterus completely⁸. The appearance of improved HSG makes up for the

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shortcomings of traditional HSG, which can show the uterine cavity more clearly by changing the body position and tilting the bulb tube.

The size and shape of⁹. However, there is still a lack of relevant research on its therapeutic effect in infertile patients.

For infertile patients, different treatment measures have different effects on tubal patency. Therefore, in order to obtain the best treatment scheme, we compared the efficacy of traditional HSG and modified HSG in infertile patients, as follows.

MATERIALS AND METHODS

Clinical Data

Altogether 110 infertile cases from March 2018 to July 2020, with an average age of 29.31 ± 3.17 years, were grouped into the observation group (OG, 58 cases) and the control group (CG, 52 cases) according to different therapies. Infertility patients confirmed as fallopian tubes abnormality were included. Those with inflammation of reproductive organs or malignant tumor, those were allergic to contrast medium, or those with severe systemic diseases were excluded. A written informed consent form was obtained from all individuals. This research conformed to the hospital ethics committee and the Declaration of Helsinki.

Therapeutic Regimen

The OG was treated with modified HSG, and all patients were given angiography 3 ~ 7 days after menstruation. The examinee was given the lithotomy position and disinfected routinely. The sterile towel was spread, and about 3 ml of normal saline was injected into the balloon through the side hole. The medical stuff should make sure that the balloon has blocked the cervix, fix the catheter, and about 15mL of 320mgI/mL iodophor, 5mg of dexamethasone and 80,000 IU of gentamicin were injected with a 20mL syringe. The filling situation of uterus and bilateral fallopian tubes was carefully observed. During this process, the patient's left anterior inclination or right anterior inclination is about 15°. If there is overlap between contrast media

and fallopian tubes, the tube was tilted to the foot side or head side, and if the distal fallopian tubes are blocked, high pressure injection was performed. After recanalization, repeated salpingography and fluid drainage were performed to observe the filling of uterine cavity. The CG was treated with conventional HSG, and the patients were in supine position. The detection method was the same as the OG, but there was no need to change the position and tilt the tube. Patients were treated with broad-spectrum antibiotics for 3 days to prevent infection, and sex life was forbidden within 1 week.

Outcome Measures

(1) The tubal patency of two groups of patients after treatment was checked and compared, and the situation included bilateral patency, unilateral patency and no patency. (2) The levels of sex hormones, including luteinizing hormone (LH), follicle stimulating hormone (FSH) and estradiol (E2), were examined and compared between the CG and the OG before and after therapy. (3) The changes of uterine volume and endometrial thickness were tested before and after therapy. (4) The individuals were followed up for one year, and the pregnancy success rate was counted and compared. (5) The adverse reactions of the CG and the OG after treatment were recorded and compared, including tubal spasm, bleeding and pain.

Statistical Method

SPSS 19.0 was applied for statistical analysis, and Graphpad 8.0 for picture visualization. Counting data were represented in percentage, and compared by χ^2 . Measurement data were represented in ($\bar{x} \pm s$), and compared by t test. Paired t test was applied for comparison before and after therapy. $P < 0.05$ indicates the difference with statistical significance.

RESULT

General Information

There was no remarkable difference in age, BMI and infertile duration between the CG and the OG ($P > 0.05$), which is comparable (Table 1).

Table 1.
Comparison of general data

factor	OG n=58	CG n=52	χ^2	P
Age (years)			0.002	0.967
≤29	31(53.45)	28(53.85)		
>29	27(46.55)	24(46.15)		
BMI(kg/m ²)			0.001	0.983
≤23	30(51.72)	27(51.92)		
>23	28(48.28)	25(48.08)		
Infertility situation			0.016	0.898
Primary infertility	35(60.34)	32(61.54)		
Secondary infertility	23(39.66)	20(38.46)		
Infertile duration	4.03±0.67	4.05±0.64	0.169	0.874
History of smoking			0.051	0.822
Yes	20(34.48)	19(36.54)		
No	38(65.52)	33(63.46)		
Tubal obstruction			0.071	0.790
Unilateral obstruction	32(55.17)	30(57.69)		
Bilateral obstruction	26(44.83)	22(42.31)		
History of drinking			0.001	0.976
Yes	18(31.03)	16(30.77)		
No	40(68.97)	36(69.23)		

Tubal Condition

After treatment, the cases of bilateral patency, unilateral patency and non-patency in the OG were 38, 18 and 2, respectively, and the tubal patency

rate was 96.55%. The cases in the CG were 25, 14 and 13, respectively, and the tubal patency rate in the CG was 75.00%, which was markedly lower than that in the OG ($P<0.05$) (Table 2).

Table 2.
Tubal condition

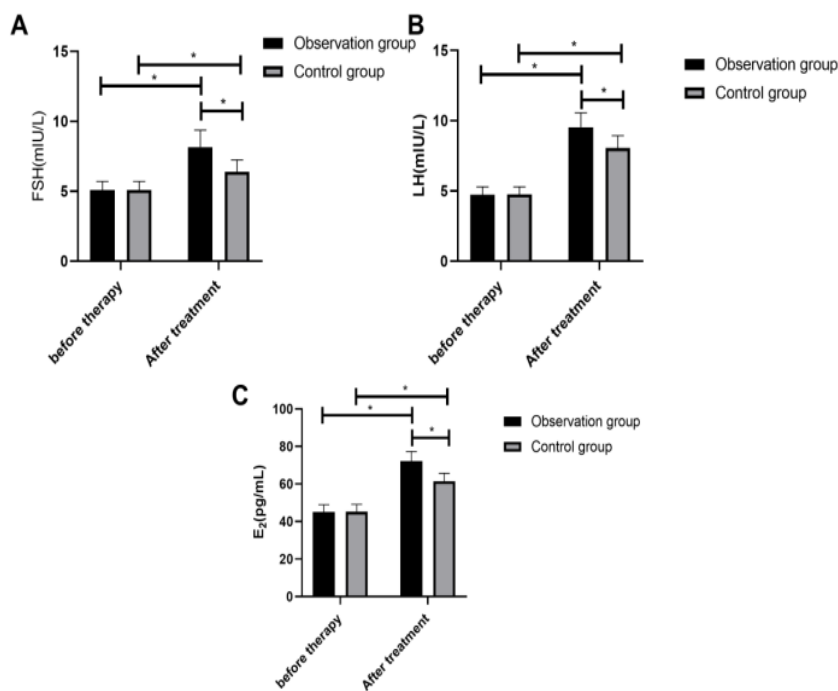
Group	OG n=58	CG n=52	χ^2	P
Bilateral patency	38(65.52)	25(48.08)	-	-
Unilateral patency	18(31.03)	14(26.92)	-	-
No patency	2(3.45)	13(25.00)	-	-
Patency rate	56(96.55)	39(75.00)	10.81	<0.001

Hormone Levels

After treatment, FSH, LH and E2 after treatment were markedly elevated compared with

those before therapy ($P<0.05$). However, those in the OG after treatment were markedly higher than those in the CG ($P<0.05$) (Figure 1).

Fig. 1.
Hormone levels



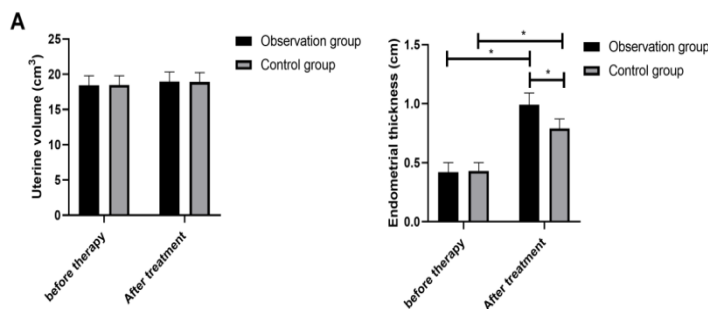
A: FSH of the CG and the OG before and after therapy; B: LH of the CG and the OG before and after therapy; C: E₂ of the CG and the OG before and after therapy. * indicates P < 0.05.

Uterine Volume and Endometrial Thickness

There was no remarkable difference in uterine volume between the OG and the CG before and after therapy (P > 0.05). The endometrial thickness

elevated markedly after treatment (P < 0.05), but the elevation of the OG was more obvious than that of the CG (P < 0.05) (Figure 2).

Fig. 2.
Uterine volume and endometrial thickness



A: uterine volume of two groups before and after therapy; B: endometrial thickness before and after therapy. * indicates P < 0.05.

Postoperative Pregnancy

All individuals were followed up for 1 year after operation. The natural pregnancy rate in the OG

(70.69%) was markedly higher than that in the CG (48.08%) (P < 0.05) (Table 3).

Table 3.

Postoperative pregnancy

Item	OG n=58	CG n=52	χ^2	P
Natural pregnancy rate	41(70.69)	25(48.08)	5.842	0.016

Adverse Reactions

The cases of tubal spasm, bleeding and pain in the OG were 1, 1 and 2 respectively, with the complication rate of 6.90%. The cases in the CG

were 3, 5 and 4 respectively, with the complication rate of 23.08%. The incidence of the OG was markedly lower than that of the CG ($P<0.05$) (Table 4).

Table 4.

Incidence of complications

complication	OG n=58	CG n=52	χ^2	P
Tubal spasm	1(1.72)	3(5.77)	-	-
Bleeding	1(1.72)	5(9.61)	-	-
Pain	2(3.45)	4(1.92)	-	-
Total incidence rate	4(6.90)	12(23.08)	5.775	0.016

DISCUSSION

With the continuous development of society, the social and family pressures faced by females are also increasing. Various factors have seriously affected the reproductive health of females, and the incidence of infertility is also increasing^{10,11}. Tubal obstruction is the main pathological factor leading to female infertility¹². Tubal patency is the premise to ensure the normal conception of women, but once the fallopian tube is blocked due to congenital or acquired reasons, it will cause infertility symptoms in patients¹³.

At present, HSG is often applied for the treatment of infertility patients caused by fallopian tube diseases. HSG refers to an examination method that injects contrast into uterine cavity, records the flow process of contrast medium through X-ray observation, displays the shape of uterine and fallopian tube cavity, and is convenient for filming and examination¹⁴. At present, as HSG has safe operation, no anesthesia, no obvious pain and high patient acceptance, it is the main therapy for examining uterine and fallopian tube diseases, and it is also a commonly applied examination mode in modern gynecological examination¹⁵. In addition, HSG has therapeutic effect. Previous studies have shown¹⁶ that HSG has a certain therapeutic effect on infertility patients with unobstructed bilateral fallopian tubes, mainly due

to the bactericidal effect of contrast media in fallopian tubes, which can not only improve the internal environment of uterus and fallopian tubes, but also inhibit the phagocytosis of monocytes on sperm, thus increasing the success rate of pregnancy. Our results showed that the tubal patency rate in the OG was markedly higher than that in the CG, indicating that the modified HSG has better therapeutic effect than the conventional HSG. Previous studies¹⁷ have shown that modified HSG can not only improve the obstruction caused by hydrosalpinx, but also have good applicability to patients with proximal tubal obstruction and distal tubal obstruction. The result is consistent with our observation. For infertile patients, the change of sex hormone level also has an important effect on pregnancy. FSH is a hormone secreted by pituitary gland, and its main function is to promote follicular maturation¹⁸. LH is a glycoprotein hormone secreted by basophils in the anterior pituitary gland, which can mainly promote ovulation in women¹⁹. E2, as the main estrogen, can not only promote and regulate the normal development of female sexual organs, but also be an important hormone to maintain female sexual function and secondary sexual characteristics²⁰. Our results revealed that the levels of FSH, LH and E2 after treatment were markedly higher than those before therapy, but those in the OG improved more obviously than those in the CG. This suggested

that modified HSG could improve estrogen level more obviously.

The thickness of endometrium is also affected by fallopian tubes obstruction. The thickness of endometrium has a certain influence on the process of conception. Some studies ²¹ show that the implantation of embryo requires a certain thickness of endometrium, and abnormally thin endometrium is not conducive to female conception. Our research results show that the endometrial thickness of patients in both groups elevated markedly after treatment, but the thickness of the OG elevated more obviously than that of the CG. The reason may be that the contrast medium applied in modified HSG can also promote the growth of nerve cells, which can enhance the thickness of endometrium to a certain extent ²². It also suggests that the modified HSG can improve endometrial thickness better than the traditional HSG. Then we followed up the individuals for one year, and recorded the pregnancy situation of the CG and the OG. The results showed that the pregnancy rate of the OG was markedly higher than that of the CG, which also suggested that modified HSG had a more remarkable effect on improving infertility. Finally, we recorded the occurrence of adverse reactions of the CG and the OG of patients after treatment. The results showed that the incidence in the OG was markedly lower than that in the CG, indicating that modified HSG had higher safety for the treatment of infertile patients. Previous studies have shown that modified HSG mainly applies contrast medium to compress fallopian tubes, to form the internal fluid pressure, and to effectively unblock the fallopian tube of the patient. The modified HSG can alleviate the adverse reactions such as spasm, pain and bleeding of fallopian tube caused by conventional HSG, and the treatment effect is remarkable, which can also meet the pregnancy needs of patients.

To sum up, the modified HSG can not only effectively improve the pregnancy situation of patients, but also has higher safety compared with the traditional HSG, which is worth popularizing in clinic. There are also some limitations. Firstly, as the number of cases we included is relatively small, our experimental result still need to be

demonstrated by large sample experiments in the later stage. Secondly, there are relatively few studies on improving HSG at present, so our conclusion lacks enough references. However, in the later stage, we will further increase the sample to demonstrate our conclusion.

REFERENCES

1. Kim Young Ran, White Nicole, Bräunig Jennifer et al. Per- and poly-fluoroalkyl substances (PFASs) in follicular fluid from women experiencing infertility in Australia.[J]. *Environ Res*, 2020, 190: 109963.
2. Shinohara Satoshi, Hirata Shuji, Suzuki Kohta, Association between infertility treatment and intrauterine growth: a multilevel analysis in a retrospective cohort study.[J]. *BMJ Open*, 2020, 10: e033675.
3. He Yanni, Geng Qiang, Liu Hongmei et al. First experience using 4-dimensional hysterosalpingo-contrast sonography with SonoVue for assessing fallopian tube patency.[J]. *J Ultrasound Med*, 2013, 32: 1233-43.
4. Huang Chen, He Xueping, Luo Wenfeng et al. Combined chitosan and Dan-shen injection for long-term tubal patency in fallopian tube recanalization for infertility.[J]. *Drug Deliv Transl Res*, 2019, 9: 738-747.
5. Hajishafiha Masomeh, Zobairi Taher, Zanjani Vahide Rasoli et al. Diagnostic value of sonohysterography in the determination of fallopian tube patency as an initial step of routine infertility assessment.[J]. *J Ultrasound Med*, 2009, 28: 1671-7.
6. Agrawal Namita, Fayyaz S, Can hysteroscopic mediated chromopertubation obviate the need for hysterosalpingography for proximal tubal blockage?: An experience at a single tertiary care center.[J]. *J Gynecol Obstet Hum Reprod*, 2019, 48: 241-245.
7. Tsuji Isao, Ami Kazumi, Fujinami Nahoko et al. The significance of laparoscopy in determining the optimal management plan for infertile patients with suspected tubal pathology revealed by hysterosalpingography.[J]. *Tohoku J Exp Med*, 2012, 227: 105-8.
8. Dreyer Kim, Out Renée, Hompes Peter G A et al. Hysterosalpingo-foam sonography, a less painful procedure for tubal patency testing during fertility workup compared with (serial) hysterosalpingography: a randomized controlled trial.[J]. *Fertil Steril*, 2014, 102: 821-5.
9. Shalev J, Krissi H, Blankstein J et al. Modified hysterosalpingography during infertility work-up: use of contrast medium and saline to investigate mechanical factors.[J]. *Fertil Steril*, 2000, 74: 372-5.
10. Li Yun-Zhi, Qiu Jie, Ma Bin et al. The role of diagnostic magnetic resonance hysterosalpingography in the evaluation of fallopian tubal occlusion of female infertility: A meta-analysis.[J]. *Clin Imaging*, 2021, 72: 11-18.
11. Hajishafiha Masomeh, Zobairi Taher, Zanjani

- Vahide Rasoli et al. Diagnostic value of sonohysterography in the determination of fallopian tube patency as an initial step of routine infertility assessment.[J] .J Ultrasound Med, 2009, 28: 1671-7.
- 12.Gao Y B,Yan J H,Yang Y D et al. Diagnostic value of transvaginal four-dimensional hysterosalpingo-contrast sonography combined with recanalization in patients with tubal infertility.[J] .Niger J Clin Pract, 2019, 22: 46-50.
- 13.Chen Fenhong,Quan Juan,Huang Pintong et al. Hysterosalpingo-Contrast Sonography With Four-Dimensional Technique for Screening Fallopian Tubal Patency: Let's Make an Exploration.[J] .J Minim Invasive Gynecol, 2017, 24: 407-414.
- 14.Dreyer Kim,Out Renée,Hompes Peter G A et al. Hysterosalpingo-foam sonography, a less painful procedure for tubal patency testing during fertility workup compared with (serial) hysterosalpingography: a randomized controlled trial.[J] .Fertil Steril, 2014, 102: 821-5.
- 15.Jitchanwichai Akarawit,Soonthornpun Karanrat,Effect of Premedication Hyoscine-N-Butylbromide before Hysterosalpingography for Diagnosis of Proximal Tubal Obstruction in Infertile Women: A Randomized Double-Blind Controlled Trial.[J] .J Minim Invasive Gynecol, 2019, 26: 110-116.
- 16.Waheed Khawaja B,Albassam Muneera A,AlShamrani Alaa-Ali G et al. Hysterosalpingographic findings in primary and secondary infertility patients.[J] .Saudi Med J, 2019, 40: 1067-1071.
- 17.Amer Mohamed I M,Ahmed Mortada E,Hassan Dalal A,Hysteroscopic tubal occlusion using iso-amyl-2-cyanoacrylate in patients with hydrosalpinx.[J] .J Obstet Gynaecol Res, 2018, 44: 2174-2180.
- 18.Xu Huiyu,Shi Li,Feng Guoshuang et al. An Ovarian Reserve Assessment Model Based on Anti-Müllerian Hormone Levels, Follicle-Stimulating Hormone Levels, and Age: Retrospective Cohort Study.[J] .J Med Internet Res, 2020, 22: e19096.
- 19.Geng Yudi,Lai Qiaohong,Xun Yang et al. The effect of premature luteinizing hormone increases among high ovarian responders undergoing a gonadotropin-releasing hormone antagonist ovarian stimulation protocol.[J] .Int J Gynaecol Obstet, 2018, 142: 97-103.
- 20.Zhang Wanlin,Ma Yefei,Xiong Yujing et al. Supraphysiological serum oestradiol negatively affects birthweight in cryopreserved embryo transfers: a retrospective cohort study.[J] .Reprod Biomed Online, 2019, 39: 312-320.
- 21.Babayev Elnur,Matevossian Karine,Hensley Caroline et al. Baseline Endometrial Thickness or Endometrial Thickness Change in Response to Estrogen Is Not Predictive of Frozen Embryo Transfer Success in Medicated Cycles.[J] .Reprod Sci, 2020, 27: 2242-2246.
- 22.Tomic Vlatka,Kasum Miro,Vucic Katarina,Impact of embryo quality and endometrial thickness on implantation in natural cycle IVF.[J] .Arch Gynecol Obstet, 2020, 301: 1325-1330.