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Severe Pain and Postoperative Effects during Hysterosalpingography: A Meta-Analysis

#ShengPan Jiang ¹, #Shan Gao ², *YiQing Tan ¹, *Qian Yang ³, Tao Zhou ¹, ShiLin Zheng ¹, WenFeng Lei ¹, FuHua Wang ¹, Xuan Liu ¹

- Department of Interventional Medicine, Wuhan Third Hospital, Tongren Hospital of Wuhan University, Wuhan, Hubei Province, 430074, China
- 2. Department of Anesthesiology, Wuhan Third Hospital, Tongren Hospital of Wuhan University, Wuhan, Hubei Province, 430074, China
- 3. Department of Traditional Chinese Medicine, Wuhan Third Hospital, Tongren Hospital of Wuhan University, Wuhan, Hubei Province, 430074, China

*Corresponding Authors: Emails: tanyiqing072@163.com, yangqian1085@hotmail.com

These authors contributed equally to this work

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Abstract

Background: We aimed to evaluate the impact of pain on patients during Hysterosalpingography (HSG). **Methods:** PubMed, PMC and other journals were searched for randomized controlled trials (RCTS) on HSG. Appropriate articles were selected for inclusion and reasonable exclusion according to keywords. Following a thorough review of the relevant literature, the process of literature screening was conducted in accordance with the aforementioned criteria. The methodological quality of the studies was assessed using the risk of bias assessment tool developed by the Cochrane Collaboration. Meta-analysis was conducted using RevMan 5.4.1 software.

Results: Twelve studies were included, including 1530 cases in the experimental group and 1545 cases in the control group. The literature summarizes the basic information of patients during HSG and makes statistics on the differences in visual analog scale (VAS) and pain perception. The findings from the HSG examination revealed a lack of significant association between patients' pain sensation and their age and BMI. However, the duration of pregnancy in patients decreased following HSG treatment (95%CI (-18.84 to -3.58), P=0.004).Compared with conventional testing, HSG could effectively reduce the pregnancy time of patients (95%CI (-18.84, -3.58), P=0.004), reduce the VAS of patients (95%CI (-4.73, -1.51), P=0.0001), and increase the number of patients without pain (95%CI (1.80, 10.43), P=0.001).

Conclusion: During the HSG examination, acceptable pain avoidance is generated and can be relieved over time. At present, there is no effective alternative method, so the patient should cooperate with the doctor to complete the examination, to relieve the pain.

Keywords: Hysterosalpingography (HSG); Severe pain; Visual analog scale; Meta-analysis

Introduction

In clinical settings, fallopian tube disease is a prevalent factor contributing to female infertility, constituting approximately 30%-40% of cases (1). Common diagnoses associated with this condi-



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tion include fallopian tube obstruction, hydrosalpinx, tubal adhesion, and tubal patency. The primary cause of fallopian tube obstruction is often attributed to complications arising from uterine cavity operations combined with fallopian tube inflammation. Additionally, a history of incomplete abortion and artificial abortion may further contribute to this condition. However, a considerable number of them are caused by other reasons, such as vaginitis, cervicitis, endometritis, appendicitis, ascending infection of tuberculosis pathogens, unclean sex life, abdominal surgery and other factors can also lead to fallopian tube obstruction (2).

Some infertile patients, who have never been pregnant, are not pregnant after several months of monitoring ovulation, and they are advised to have their fallopian tubes checked for patency. At present, the commonly used methods to check the patency and function of the fallopian tube are HSG, hysteroscopic fallopian tube patency test, and ultrasound fallopian tube patency test (3).

HSG is the injection of iodine contrast agent directly from the cervical canal into the uterine cavity, and then through the uterine cavity to the fallopian tube. The patency of the uterine cavity and fallopian tube is observed under X-ray fluoroscopy (4). Generally, 3 to 7 days after the menstrual period, sexual intercourse is forbidden, and angiography is performed. The uterus and fallopian tube were shown by the contrast agent, and the fallopian tube patency and the distribution of contrast agent in the pelvic cavity were observed by another X-ray film the next day. This is a widely used traditional examination method, which can observe the uterine cavity and fallopian tube lumen, and has a dredging effect at the same time (5).

HSG is an emerging technology in recent years, which can not only observe the uterine cavity and fallopian tube cavity, but also avoid radiation exposure and iodine allergy (6). Ultrasound microbubble contrast agent is injected into the uterine cavity under the uterine cavity, and the tubal patency can be evaluated and the uterine and pelvic lesions can be observed through ultrasound scanning. It has the advantages of non-

invasiveness, safety, accuracy, and unlimited postoperative pregnancy time. HSG generally has a feeling of swelling and pain. Because this is an invasive examination, it is a kind of surgical nature of gynecology. There was a feeling of pain in the lower abdomen like dysmenorrhea, but the pain was within the tolerable range. Pain is a common complication of HSG, but it can be relieved by intramuscular anesthetics before operation (7). Many people feel abdominal pain, even difficult to deeply, and accompanied by nausea, vomiting, fatigue and weakness, severe cases will syncope, shock. The contrast tube penetrates deep into the uterine cavity and irritates the hysterofallopian tubes causing spasms. Fallopian tube obstruction or unobstructed, patients with poor pain tolerance can cause pain. After proper rest, the pain symptoms can be relieved spontaneously. Patients were advised to be observed for 1 hour after surgery before leaving the hospital.

Related work

About 15% of married women suffer from infertility, of which 25%-30% are caused by tubal factors. Therefore, the evaluation of fallopian tube function is of great significance for the treatment of infertility (8). At present, the methods to determine fallopian tube patency include fallopian tube ventilation or hydrotubation, HSG, laparoscopic or hysteroscopic hydrotubation, CT, MRI, etc. HSG is a minimally invasive examination, with an accuracy of 98% and a therapeutic effect (9). HSG is the most commonly used examination method to find out whether the fallopian tube is unobstructed, the degree of unobstructed and the specific site of obstruction. In many aspects, it cannot be replaced by ultrasound, CT, MRI, hysteroscopy, laparoscopy, salpingoscopy and so on (10).

Materials and Methods

Document inclusion criteria

1) Clinical trials of HSG examination. 2) randomized controlled trial. 3) The experimental group was examined by HSG, and the control

group was examined by other methods. 4) The pregnancy time, visual analog scale (VAS) and incidence of pain were compared between the two groups.

Literature selection criteria

1) Patients requiring HSG examination; 2) Randomized controlled trial. 3) Clear indicators; 4) The detection method is reliable; 5) Consistent indicators.

Retrieval strategy

Key words: HSG; Severe pain; VAS; Metaanalysis. Databases: PubMed, PMC, Scopus and Web of Science.

Quality evaluation

The collaborative network bias risk assessment tool was used to evaluate the quality of the literature, mainly including: 1) No difference between the samples; 2) Random sample allocation. 3) Double-blind method; 4) The detection method is reliable; 5) No selective data; 6) Other deviations. Jiang and Gao independently screened the literature and extracted the data. If there is disagreement, they discuss it or a third researcher is involved in the negotiations. The main contents of data extraction were first author, publication year, basic information of patients and important indicators: pregnancy time, VAS and incidence of pain.

Statistical method

RevMan 5.4.1 software was used to analyze statistically the effective data in the selected literature. In this paper, the possibility of publication bias between studies is low when the funnel plot is bilaterally symmetric. Data results if P < 0.1 and $I^2 > 50\%$, indicating that there is great heterogeneity among the research results. If P > 0.1 and $I^2 < 50\%$, non-heterogeneity was considered to exist. The fixed-effect model (the Mantel–Haenszel method) and the random effects model (the DerSimonians–Laird method) were used in the meta-analysis. P < 0.05, indicating a statistically significant difference.

Results

Literature search results

Fort six relevant articles were retrieved from PubMed and PMC. Non-controlled clinical trials were excluded, and 14 studies were left. Then, through the title, abstract and key words of the literature, 12 articles whose research content was consistent with this study were selected. The quality of 12 articles was assessed, and the detailed process is shown in Fig. 1. Table 1 shows the included studies, including authors, year of publication, sample size and key indicators.

Table 1: Basic characteristics of the included literature

Included literature		r of samples l\Control group	Indicators
Hikmet Hassa 2014 (11)	50	55	Duration of infertility, VAS
Iwona Szymusik 2014 (12)	80	89	Duration of infertility, VAS
A A Peters 2015 (13)	49	42	VAS,
Aytekin Tokmak 2015 (14)	84	25	Duration of infertility, VAS, No pain
J Shalev 2000 (15)	40	38	Duration of infertility
F Moro 2012 (16)	408	408	VAS, No pain
G Ayida 1996 (17)	34	32	No pain
Maryam Gharib 2015 (18)	32	32	Duration of infertility, VAS
Scott G. Chudnoff 2015 (19)	366	366	Duration of infertility, No pain
N van Welie 2019 (20)	199	201	Duration of infertility, No pain
Nienke van Welie 2022 (21)	54	51	Duration of infertility, VAS, No pain
Ning Zhang 2021 (22)	134	206	Duration of infertility, VAS

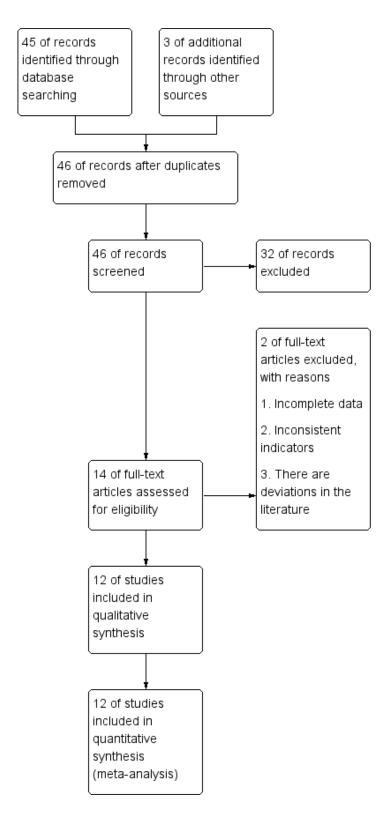


Fig.1: Flow chart of literature search

The publication bias analysis

After collecting and screening the literature, publication bias was used to analyze the quality of the

12 included studies. The results, as shown in Fig. 2, showed that the risk of bias of the 12 articles was small and the articles had reference value.

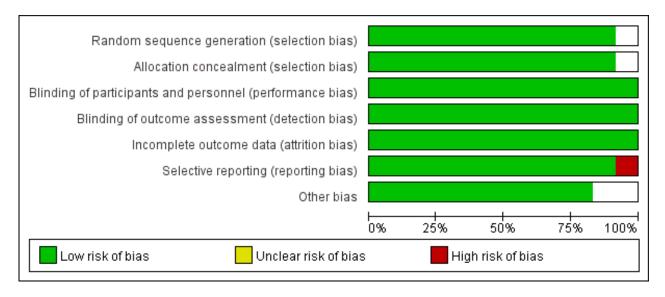


Fig. 2: The publication bias analysis

Meta-analysis results Analysis of sample number change between the two groups

The number of patients included in this study is shown in Fig. 3. The differences between the two groups were compared through statistics and analysis. No patients dropped out during the trial. As shown in Fig. 4, there was no statistical heterogeneity between the two groups, and the selected literature has reference value (95%Cl (1.00, 1.00), $I^2=0\%$, P=1.00).

	Experimental Control		ol		Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
A A Peters 2015	49	49	42	42	3.0%	1.00 [0.96, 1.04]	
Aytekin Tokmak 2015	84	84	25	25	2.6%	1.00 [0.95, 1.06]	
F Moro 2012	408	408	408	408	26.9%	1.00 [1.00, 1.00]	•
G Ayida 1996	34	34	32	32	2.2%	1.00 [0.94, 1.06]	
Hikmet Hassa 2014	50	50	55	55	3.5%	1.00 [0.96, 1.04]	
lwona Szymusik 2014	80	80	89	89	5.6%	1.00 [0.98, 1.02]	
J Shalev 2000	40	40	38	38	2.6%	1.00 [0.95, 1.05]	
Maryam Gharib 2015	32	32	32	32	2.1%	1.00 [0.94, 1.06]	
Nienke van Welie 2022	199	199	201	201	13.2%	1.00 [0.99, 1.01]	+
Ning Zhang 2021	54	54	51	51	3.5%	1.00 [0.96, 1.04]	
N van Welie 2019	134	134	206	206	10.7%	1.00 [0.99, 1.01]	+
Scott G. Chudnoff 2015	366	366	366	366	24.1%	1.00 [0.99, 1.01]	†
Total (95% CI)		1530		1545	100.0%	1.00 [1.00, 1.00]	•
Total events	1530		1545				
Heterogeneity: Chi² = 0.00	0, df = 11 (P = 1.00)); I² = 0%	,			
Test for overall effect: Z=	$0.00 (P = \frac{1}{2})$	1.00)					0.85
		,					Favours [experimental] Favours [control]

Fig. 3: The forest plot of sample number

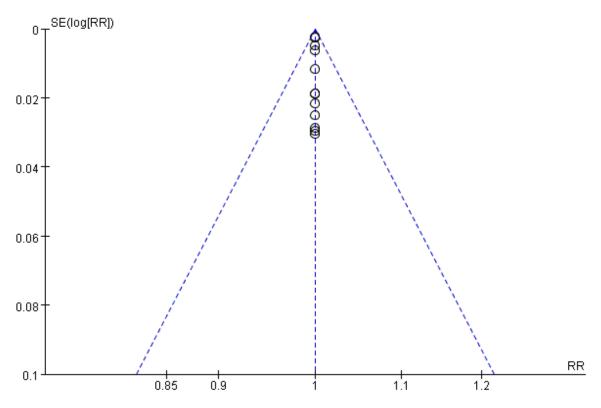


Fig. 4: The forest plot of sample number

Statistical differences in mean age and BMI between the two groups

Analysis of differences in mean age and BMI among patients enrolled in the clinical trials shows the results in Fig. 5-8. The results showed no significant differences in mean age (95%Cl (-

0.06, 0.70), $I^2=59\%$, P=0.10) and BMI (95%Cl (-0.41, 0.10), $I^2=0\%$, P=0.23) between the two groups. Therefore, there was no difference in the basic information of the patients. During the HSG examination, the pain sensation of the patients was not related to age and BMI.

	Experimental			Co	ntro	ı		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	otal Mean SD Total			Weight	IV, Random, 95% CI	IV, Random, 95% CI
A A Peters 2015	30	1	49	30	1	42	14.0%	0.00 [-0.41, 0.41]	+
Aytekin Tokmak 2015	28.5	6.4	84	28.3	5.8	25	1.8%	0.20 [-2.45, 2.85]	
F Moro 2012	34.2	4.2	408	34.6	4.2	408	12.1%	-0.40 [-0.98, 0.18]	
G Ayida 1996	33.7	4.3	34	33.7	4.4	32	2.7%	0.00 [-2.10, 2.10]	
Hikmet Hassa 2014	30	2.4	50	28	2.4	55	8.4%	2.00 [1.08, 2.92]	
lwona Szymusik 2014	31.9	4.2	80	31.7	4.1	89	5.9%	0.20 [-1.05, 1.45]	
J Shalev 2000	23.1	2.9	40	23.1	2.9	38	5.7%	0.00 [-1.29, 1.29]	
Maryam Gharib 2015	32	1	32	32	1	32	13.1%	0.00 [-0.49, 0.49]	+
Nienke van Welie 2022	33.9	3.1	199	33.7	3.2	201	11.6%	0.20 [-0.42, 0.82]	+
Ning Zhang 2021	33	2.9	54	32	2.9	51	6.9%	1.00 [-0.11, 2.11]	 • -
N van Welie 2019	31.2	5.6	134	29.8	4.7	206	6.6%	1.40 [0.26, 2.54]	
Scott G. Chudnoff 2015	31.9	4.6	366	31.9	4.6	366	11.1%	0.00 [-0.67, 0.67]	+
Total (95% CI)			1530			1545	100.0%	0.32 [-0.06, 0.70]	♦
Heterogeneity: Tau ² = 0.2	2; Chi² =	27.04	, df = 1	1 (P = 0	.005)	; I² = 59	3%	-	
Test for overall effect: Z=				•	ĺ	•			-4 -2 0 2 4
	٧.		•						Favours [experimental] Favours [control]

Fig. 5: The forest map of mean age between the two groups

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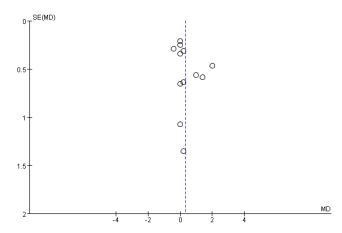


Fig. 6: The bias analysis of mean age between the two groups

	Experimental			Co	ntro	I		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
A A Peters 2015	34	1	49	34	1	42	37.0%	0.00 [-0.41, 0.41]	-
Aytekin Tokmak 2015	24.6	4.4	84	25.2	4.2	25	1.7%	-0.60 [-2.50, 1.30]	
Hikmet Hassa 2014	23.5	2.03	50	24	2	55	10.6%	-0.50 [-1.27, 0.27]	
Nienke van Welie 2022	22.2	2	199	22.4	2	201	40.9%	-0.20 [-0.59, 0.19]	
Ning Zhang 2021	24.2	2.1	54	24.3	2.1	51	9.7%	-0.10 [-0.90, 0.70]	
Total (95% CI)			436			374	100.0%	-0.15 [-0.41, 0.10]	•
Heterogeneity: Chi² = 1.5	9, df = 4	(P = 0.	81); l² =		-2 -1 0 1 2				
Test for overall effect: Z =	1.21 (P	= 0.23))	Favours [experimental] Favours [control]					

Fig. 7: The forest map of BMI of the two groups

Differences in duration of infertility between the two groups

The statistical analysis of the pregnancy time of the two groups is shown in Fig. 9 and 10. The results show that the pregnancy time of the patients was shortened after HSG treatment, and there was a statistical difference between the groups (95%Cl (-18.84, -3.58), *P*=0.004). Therefore, the clinical efficacy of HSG in the treatment of tubal infertility is significant.

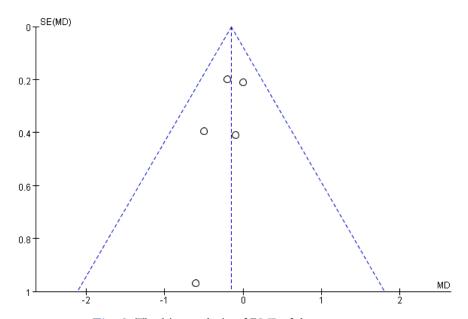


Fig. 8: The bias analysis of BMI of the two groups

	Ехре	ıtal	C	ontrol			Mean Difference	Mean Difference	
Study or Subgroup	Mean SD Total Mean SD Total V				Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	
Aytekin Tokmak 2015	33.7	3.7	84	39.2	4.3	25	11.5%	-5.50 [-7.36, -3.64]	•
Hikmet Hassa 2014	33	17	50	36	14	55	10.8%	-3.00 [-8.99, 2.99]	
lwona Szymusik 2014	29	18	80	32.2	20.4	89	10.9%	-3.20 [-8.99, 2.59]	
J Shalev 2000	31.2	15	40	35	12	38	10.8%	-3.80 [-9.81, 2.21]	
Maryam Gharib 2015	33.9	12	32	95.2	12	32	10.9%	-61.30 [-67.18, -55.42]	
Nienke van Welie 2022	19.2	16	199	19.8	15.7	201	11.4%	-0.60 [-3.71, 2.51]	†
Ning Zhang 2021	20	14.8	54	21	16.7	51	10.8%	-1.00 [-7.05, 5.05]	+
N van Welie 2019	19.2	18	134	32	12	206	11.3%	-12.80 [-16.26, -9.34]	+
Scott G. Chudnoff 2015	45	12	366	55.5	12	366	11.5%	-10.50 [-12.24, -8.76]	•
Total (95% CI)			1039			1063	100.0%	-11.21 [-18.84, -3.58]	•
Heterogeneity: Tau ² = 13	0.59; Ch	i² = 37	0.10, dt	f= 8 (P ·	< 0.00	001); l²	= 98%		100 50 100
Test for overall effect Z = 2.88 (P = 0.004)									-100 -50 0 50 100 Favours [experimental] Favours [control]

Fig. 9: The forest map of duration of infertility between the two groups

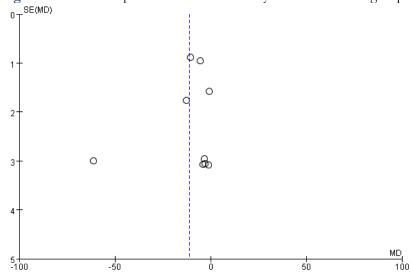


Fig. 10: The bias analysis of duration of infertility between the two groups

Differences in VAS between the two groups

During HSG, the patient may have some discomfort. VAS is the most commonly used pain assessment, so VAS was used to describe the pain of patients during HSG. The results are shown in

Fig. 11 and 12. The results showed that HSG was associated with less pain than other examination methods, and the difference was statistically significant. (95%Cl (-4.73, -1.51), P=0.0001).

	Experimental Control						Mean Difference	Mean Difference				
Study or Subgroup	Mean SD Total Mean SD Total				Weight	IV, Random, 95% CI	IV, Random, 95% CI					
A A Peters 2015	15	17	49	45	34	42	1.8%	-30.00 [-41.33, -18.67]				
Aytekin Tokmak 2015	5.9	2.5	84	7.5	2.1	25	14.0%	-1.60 [-2.58, -0.62]			-	
F Moro 2012	13	3.2	408	19	4.7	408	14.5%	-6.00 [-6.55, -5.45]			•	
Hikmet Hassa 2014	5.5	3	50	6.7	4.6	55	13.1%	-1.20 [-2.67, 0.27]			•	
lwona Szymusik 2014	4.4	2.6	80	4.61	2.59	89	14.2%	-0.21 [-0.99, 0.57]			+	
Maryam Gharib 2015	3.5	2.28	32	6.03	2.5	32	13.7%	-2.53 [-3.70, -1.36]			•	
Ning Zhang 2021	3.1	2.2	54	5.4	2.5	51	14.1%	-2.30 [-3.20, -1.40]			•	
N van Welie 2019	3.11	1.26	134	7.46	1.64	206	14.7%	-4.35 [-4.66, -4.04]			•	
Total (95% CI)			891			908	100.0%	-3.12 [-4.73, -1.51]			•	
Heterogeneity: Tau ² = 4	Heterogeneity: Tau ² = 4.58; Chi ² = 220.52, df = 7 (P < 0.00001); I ² = 97%								-100	-50	0 50	100
Test for overall effect: Z	= 3.80 (F	9 = 0.0	001)							-50 avours (experimental		100
									Fè	avours jexperimentai	ravours (control)	

Fig. 11: The forest map of VAS between the two groups

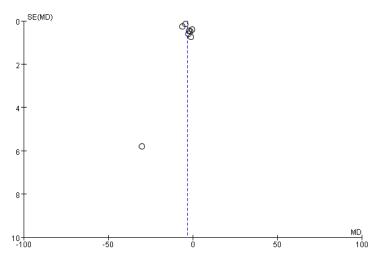


Fig. 12: The bias analysis of VAS between the two groups

Differences in number of patients with no pain between the two groups

The number of patients with small disappearance of pain after a period after HSG was counted, and the results are shown in Fig. 13 and 14. The results showed that after a period of time, the number of patients with pain disappearance in

the HSG group was more than that in the conventional method, and the difference was statistically significant (95%Cl (1.80, 10.43), *P*=0.001). Therefore, patients do not need to be overly nervous during HSG and should cooperate with doctors.

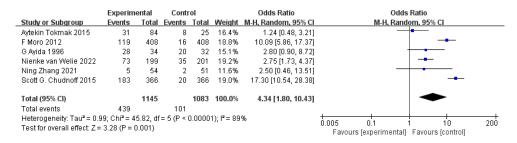


Fig. 13: The forest map of number of patients with no pain between the two groups

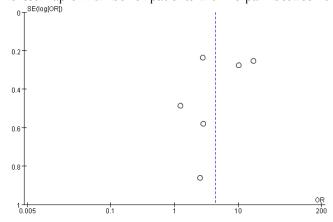


Fig. 14: The bias analysis of number of patients with no pain between the two groups

Discussion

HSG is the most commonly used method to find out whether the fallopian tube is unobstructed, the degree of unobstructed fallopian tube and the specific obstruction site (13). It can make correct diagnosis of fallopian tube obstruction with an accuracy of 98% under the operation of experienced doctors and the application of digital X-ray machine. In many aspects, it cannot be replaced by ultrasound, CT, MRI, hysteroscopy, laparoscopy, salpingoscopy and so on (23).

HSG requires cervical intubation into the uterine cavity, which is an invasive examination and will have a certain amount of pain. At the same time, any operation may have risks and complications. The main possible risk of HSG is infection. HSG is an invasive procedure in which contrast material is passed through the uterus into the pelvic cavity (24). Therefore, the relevant gynecological examination must be done before the fallopian tube examination to find out whether there is inflammation and prevent the spread of inflammation caused by the fallopian tube examination. Doctors must strictly follow the principle of aseptic operation to prevent iatrogenic infection. The temperature on the day of examination should be below 37.5 °C (2). Fallopian tube tests use X-rays to look at the distribution of contrast material. At the same time, in order to avoid confused expectations-to-be mothers do not know that they are pregnant in the case of the examination, doctors generally will routinely check blood or urine HCG before surgery. In addition, women should refrain from sexual life before and after the examination of the month within 2 weeks to prevent pregnancy in the month, and avoid the phenomenon of inflammation caused by sexual life, causing pain and bleeding. The uterus belongs to the pelvic organ, which is innervated by sympathetic and parasympathetic nerves, as well as rich sensory nerve distribution. The nerve endings of the uterine neck are more sensitive (25). Cervical intubation during HSG and dilation of the uterine cavity during HSG may stimulate nerve endings distributed in these areas. Most women are able to tolerate these stimuli through the self-regulation of the nervous system. However, there are also a small number of patients due to the poor stability of the autonomic nerve, the vagus nerve reflex is strong, may appear nausea, vomiting, dizziness, chest tightness, shortness of breath, pale face, sweating, limbs cold and other symptoms (26). Even a drop in blood pressure, arrhythmia, etc., serious cases may also appear fainting, convulsions and other symptoms. In general, in addition to infection, lower abdominal pain is the most common complication of HSG. This is mainly caused by the contrast agent entering the uterus and causing uterine contractions. When this occurs, the main symptom is abdominal pain in the lower abdomen. In addition, if the contrast agent is overflowing, it will also cause pelvic irritation, resulting in abdominal pain (27). According to the results, compared with conventional testing, HSG can effectively reduce the pregnancy time of patients (95%CI (-18.84, -3.58), P=0.004), reduce the VAS of patients (95%CI (-4.73, -1.51), P=0.0001), and increase the number of patients without pain (95%CI (1.80, 10.43), P=0.001). Normally, during the procedure, the oviductradiography catheter needs to be inserted into the cervix and then secured with a balloon. During this procedure, the patient may have some mild discomfort, and there may be some falling sensation in the lower abdomen as the contrast material enters the uterus. Most people can tolerate it. If the patient is too nervous, or tubal blockage is more serious, this feeling will be more intense than normal people (28). Therefore, although there will be some discomfort in HSG, it is not very painful in fact, and most patients can bear it. It is not necessary to do painless. Of course, different constitutions, pain tolerance is also different, if the pain is unbearable in the process, we must communicate with the doctor in time.

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Conclusion

During the HSG examination, acceptable pain avoidance is generated and can be relieved over time. At present, there is no effective alternative method, so the patient should cooperate with the doctor to complete the examination, to relieve the pain.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Acknowledgements

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Conflict of interests

The authors have no conflicts of interest to declare.

Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

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