An Impact of Suspected Peritubal Adhesions by Hysterosalpingography on Outcomes of Intrauterine Insemination

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Objective To assess the fertility prospect of women with suspected peritubal adhesions diagnosed by hysterosalpingography (HSG) treated with intrauterine insemination (IUI).

Methods The study group consisted of 93 patients diagnosed as bilateral suspected peritubal adhesions by HSG, and 175 patients with no tubal pathology were classified as control group. A total of 496 cycles of IUI were finished in 268 infertile women.

Results There were no differences in basic clinical parameters between the two groups. Cumulative pregnancy rates after two cycles of IUI were 19.4% for the study group, and 34.3% for the control. Cumulative pregnancy rate in the women with abnormal contrast media loculation was significantly lower than that in women of the control (7.4% vs 34.3%, P=0.037). The cumulative pregnancy rates were similar between the women with abnormal tubal contour and the normal ones (36.7% vs 34.3%, P=0.800).

Conclusion Suspected peritubal adhesions in HSG were worthy more attention, since the outcome of IUI in women with loculation of contrast material, combined with or without abnormal tubal contour resulted in a significantly lower pregnancy rate than the normal ones. IUI should be delayed before tubal patency was confirmed during these patients.

Key words: hysterosalpingography; peritubal adhesion; ovulation induction; intrauterine insemination

This study was funded by Special Foundation for Outstanding Young Teachers in Higher Education Institutions of Shanghai (2012)
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Tubal assessment is one of the most important tests, because pathologic tubal conditions account for 30%–40% cases of infertility\textsuperscript{[1,2]}. In most patients, hysterosalpingography (HSG) is still the first-line test used to determine tubal patency, despite the arrival of newer tubal assessment tests, especially in developing countries.

As the success of assisted reproductive techniques improves, \textit{in-vitro} fertilization (IVF) has gradually replaced tubal surgery as the treatment of choice for tubal subfertility in many countries. It has also become a good choice for most of the causes of subfertility\textsuperscript{[3,4]}. Therefore, fertility prospects assessment turns to be more important than estimating the seriousness of the morphological abnormalities before referring the couple for IVF treatment.

As to the diagnosis of HSG, the management of women with bilateral tubal blockage or at least one normal tubal passage is clear and straightforward, for lots of studies showed that fertility prospects were significantly reduced in patients with bilateral tubal blockage, whereas slightly impaired in the unilateral ones\textsuperscript{[5,6]}. While, treatment is vague for patients with suspected peritubal adhesions: abnormal tubal contour or loculation of contrast media in the peritubal zone. It is unknown whether fertility prospects are affected in these patients. Up to date, there is scarce research related to this problem available. Therefore, the objectives of the present study were to assess the correlation between HSG results showing suspected peritubal adhesions and pregnancy rate (PR) for intrauterine insemination (IUI), and to evaluate the probability that these HSG findings predicting poor fertility prospects.

\section*{Materials & Methods}

\subsection*{Patient selection}

We collected consecutive infertile women who did HSG, and followed with treatment of IUI within one year in our hospital between January 1, 2009 and December 31, 2011. At least two cycles of IUI were completed, unless pregnancy occurred in the first cycle. This was a retrospective analysis of standard procedures in assisted reproduction. All patients initially underwent routine evaluation which included a complete history and physical examination, semen analysis and hormonal assessment. This study included patients who met the following criteria: 1) infertility diagnosis according to WHO definition; 2) woman’s age $\leq 38$ years old; 3) normal ovarian reserve (basal FSH$<12$ mIU/ml); 4) absence of severe sperm pathology (a quantity of $\geq 5 \times 10^6$ of motile spermatozoa or donor spermatozoa); 5) without previous pelvic operation; 6) no IVF or IUI treatment history; 7) without ovary and uterus organic disease and severe general diseases; 8) excluding tubal occlusion or hydrosalpinx.

\subsection*{Procedure of HSG}

HSG processes were done by three experienced reproductive endocrinologists. All the
HSG images were recalled and reinterpreted by one radiologist according to the specific radiographic criteria[7]. First of all, normal HSG criteria were defined as a normal uterine cavity, no evidence of tubal occlusion, normal fallopian tube contour, and free bilateral spillage of the contrast media into the peritoneal cavity. Patients with tubal occlusion were excluded from the study. HSG was classified as suspected abnormal pathology when bilateral tubers were demonstrated: 1) abnormal tubal contour or position; 2) loculation of contrast media in the peritoneal cavity; or 3) both of the abnormalities above (Figure 1).

**Ovarian stimulation and IUI procedure**

Patients with patency tuber were suggested for IUI treatment. On day 3 of the menstrual cycle, patients were treated with a commencement dose of 37.5–75 IU hMG (Menotrophin, Livzon, Zhuhai, China) or recombinant FSH (Gonal-F; Merk-Serono, Geneva,
Switzerland) in a step-up process. When the leading follicle reached 18–20 mm in diameter, 5 000 IU of hCG (Chorionic Gonadotrophin for Injection, Livzon, Zhuhai, China) was given and a single IUI was randomly performed 24–36 h after hCG administration. Serum $\beta$-hCG test was performed at 14 d after insemination to determine the biochemical pregnancy. A clinical pregnancy was defined as the presence of an embryonic sac and fetal heart beat on ultrasound (at 6 weeks after insemination). The first two cycles of IUI outcomes were taken into study.

**Statistical methods**

The statistical program SPSS11.5 was used for statistical analysis. Results were expressed as means ± SD ($\bar{x}$ ± s). Continuous variables were analyzed using Student’s $t$-test, and the $\chi^2$ test was used for categorical variables. Logistic regression was used to compare cumulative PRs. A two-tailed analysis was performed, and differences were considered statistically significant at $P<0.05$.

**Results**

In the study period, a total of 273 consecutive women were approached according to the included criteria. Five of them who abandoned the sub-fertility treatment after one cycle of IUI were excluded for further analysis because of spontaneous pregnancy ($n$=1), and personal factor ($n$=4). During the 268 patients, the mean age of the patients was 29.6 ± 3.8 (22–38) years old. The mean infertility duration was 3.0 ± 1.8 (1–8) years. Infertility was reported as primary and secondary by 178 (66.4%) and 90 (33.6%), respectively.

According to the HSG results, 93 who showed bilateral tubal suspected peritubal adhesions were classified as study group, and 175 were regarded as control group. There were no differences in basic clinical parameters between the two groups (Table 1). The cumulative PR per patient was significantly lower in study group than in the control [19.4% (18/93) vs 34.3% (60/175), $P=0.011$]. The clinical PR per cycle was also significantly lower in study group than in the control [10.2% (18/176) vs 18.8% (60/320), $P=0.014$].

The binary logistic regression analysis evaluated the correlation between the mainly clinical parameters, including the HSG results, and the cumulative PRs for two cycles of IUI. Only the HSG results and the body mass index (BMI) were found to be predictors for the PR. Adjusted for the BMI, the cumulative PR in the women with abnormal contrast media loculation was significantly lower than in women of the control [7.4% (2/27) vs 34.3% (60/175), respectively; $P=0.037$; $OR=0.279$; 95%CI: 0.084–0.93]. So did the subgroup of women who showed abnormal tubal contour and abnormal contrast media loculation in the same HSG images [13.9% (5/36) vs 34.3% (60/175), respectively; $P=0.017$; $OR=0.14$; 95%CI: 0.027–0.70].

The cumulative PR was similar between the women with abnormal tubal contour and
the normal ones [36.7% (11/30) vs 34.3% (60/175), respectively; \( P = 0.800; \text{OR} = 0.901; 95\% \text{ CI: 0.40–2.02} \)](Figure 2). No complications were registered during and after IUI.

**Discussion**

Peritubal adhesion is a major factor for subfertility. It would alter the normal anatomic relationship between tube fimbriae and ovary, and interfere in the normal capture and transport
of the ovum. The presence of convoluted fallopian tubes and loculation of the contrast material around the ampullary portion of the tubes were regarded as the most representative characteristics of peritubal adhesions in the HSG images\[7\]. While, there was few research directly dealing with the effect of these “suspected peritubal adhesions” findings in the HSG on fertility ability. In our study, the cumulative PRs of two consecutive IUI cycles in women with “suspected peritubal adhesions” diagnosed by HSG were studied. Results showed a relationship between the cumulative PR and the types of tubal pathology in HSG, and it was suggested that IUI treatment for these women with contrast medium loculation was inferior, for the cumulative PRs of two IUI cycles were only 7.4%.

As IVF technique becomes an efficacious treatment for persistent infertility due to kinds of causes, the choice for IVF-embryo transfer does not depend on the detection for morphological abnormalities, but the fertility prognosis. Therefore, an ideal tubal assessment test must be powerful in predicting fertility outcome. It was reported that HSG and laparoscopy had a comparable predictive capacity for natural conception recently\[8\].

It is still unsure that the direct relationship between the suspected peritubal adhesions of HSG and the fertility prospects. Therefore, the choice of management for these patients is vague. The clinicians would choose one of belows: 1) a period of expectant management; 2) IUI to achieve pregnancy; 3) laparoscopy for further assessment; or 4) referring to IVF to bypass the problem. In the studies of the adhesion found by laparoscopy, the results showed that the presence of adhesions reduced fertility prospects on the same order as unilateral tubal occlusion, with relative risks of 0.74 (95%CI: 0.57–0.98) and 0.73 (95% CI: 0.39–1.40), respectively\[9\]. There was no study up to now assessing directly the effect of peritubal adhesions radiographic signs of HSG on the fertility prospects. It is probably because of the shortage of publicly accepted criteria for peritubal adhesion in HSG. The following signs were once identified as radiographic findings corresponding to peritubal disease\[7\]: convoluted tube, vertical position of the tube, loculation of spillage of contrast medium in peritoneum, halo effect, and fixed laterodeviation of the uterus. It was reported that hysterosalpingographic accuracy in peritubal adhesion diagnosis can be improved by taking into account more than one of the reported radiographic signs. This criterion (no sign or one sign is a normal radiographic result) improved the overall accuracy of HSG in patent tubes (89.2%), reducing false-positive results from 82.3% to 11.7% with an acceptable rate of false-negative diagnoses (9%)\[10\].

As peritubal adhesions most commonly manifest as loculation of the contrast material around the ampullary portion of the tube, and abnormal tubal contour including convoluted tube and vertical position of the tube. Our study focused on these two kinds of radiographic signs, and the definition of suspected peritubal adhesions was limited to two-sided abnormal
radiographic signs. The result showed a significant lower cumulative PR of IUI in study group than in the control, which suggested patients with “suspected peritubal adhesion” radiographic signs should be treated differently from these normal ones.

In the subgroups of study group, the HSG findings of bilateral abnormal tubal contour had a comparable cumulated PR with those of normal tubes, whereas the findings of two-sided loculation of the contrast material were related to a reduced cumulated PR for IUI. Peritubal adhesions prevent contrast material from flowing freely around the bowel loops and most commonly manifested as loculation of the contrast material around the ampullary portion of the tube. So the poor results in cases with bilateral contrast material loculation represented in the HSG were not surprising. While, the good results in cases of bilateral abnormal tubal contour, as found in our study, could be explained as: 1) the confusion of patients with convoluted tube and vertical position of the tube; 2) the position of ovaries did not show in the HSG.

It is generally agreed that laparoscopy can be delayed after normal HSG. Tanahatoe et al.[11] reported that laparoscopy revealed abnormalities that resulted in changed treatment decisions in 25% of the patients who would normally have been scheduled for IUI. The changed treatments mainly concerned surgery for minimal/mild endometriosis and periaudnexal adhesions. It was suggested that surgery was probably efficacious in improving fertility for all stages of endometriosis. Therefore, as to cases with suspected peritubal adhesion in HSG, which were found to be associated with poor IUI outcomes in this study, diagnostic laparoscopy for further assessment might be reasonable[12].

In conclusion, we suggest that patients with suspected peritubal adhesions in HSG are worthy more attention, since they are probably associated with a low pregnancy rate when treated with IUI. In women with bilateral pathologies manifested as loculation of contrast material, combined with or without abnormal tubal contour, IUI should be delayed before tubal patency confirmed. Further prospective randomized studies are needed on the validation of IUI in patients with suspected peritubal adhesion found in HSG.

References

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(Received on February 15, 2013)