Effect of chitosan-assisted combination of laparoscope and hysteroscope on the levels of IFN-γ and ICAM-1 in treatment of infertility caused by obstruction of fallopian tubes

Changying Liao1*, Zuolong Wang2*, Hongmei Li3, Fengrong Zhao1, Ling Ling1*

1 Department of Obstetrics and Gynecology, Chongqing Jiangbei District Hospital of Traditional Chinese Medicine, Chongqing400020, China
2 Department of Clinical Laboratory, Chongqing Jiangbei District Hospital of Traditional Chinese Medicine, Chongqing400020, China
3 Reproductive Medicine Centre, Chongqing Angel Maternity Hospital, Chongqing 401120, China

#They contributed equally to this work.

ARTICLE INFO

Original paper

Article history:
Received: February 15, 2023
Accepted: April 13, 2023
Published: April 30, 2023

Keywords:
Fallopian tube obstruction, infertility, bifocal surgery, chitosan, IFN-γ, ICAM-1

Doi: http://dx.doi.org/10.14715/cmb/2023.69.4.15

Copyright: © 2023 by the C.M.B. Association. All rights reserved.

Introduction

Obstruction of fallopian tubes, as a common disease in the clinical gynecological department, refers to the partial or total obstruction of fallopian tubes caused by inflammation, pelvic adhesion and infection and is also the major cause of female infertility (1). In an early stage, obstruction of the fallopian tubes usually presents no evident symptoms, but some patients may demonstrate infectious symptoms in the reproductive tract, including increased vaginal secretion, thickened adnexa area, mass formation and pains in the lower belly (2-3). Published literatures (4-5) have already confirmed that inflammatory cytokines can stimulate the oviductal mucosa to induce a series of pathological changes, like edema, effusion or congestion, and such changes, with the abundant lymphocytes and plasma cells under the mucosa of the oviductal wall, could further induce the fibrotic responses, including the thickening of wall and damage to the functions of wriggling and contraction of epithelium, thereby disturbing the abilities of infundibulum to pick up and transport the egg, eventually triggering infertility. The operation remains the major strategy in clinical treatment for infertility caused by occlusion of fallopian tubes in recent years, and the combination of hysteroscope and laparoscope is widely accepted by clinicians and patients due to the minimal invasion, rapid recovery and painlessness. However, the operation can only dredge the occluded fallopian tubes to restore the normal anatomical structure, yet remains hopeless in dealing with the changes in the microenvironment, including the pathological inflammation-caused injury and adhesion (6). Chitosan, as the sole cationic biological polysaccharide, is excellent in biological adhesion, antibacterial activity and compatibility and performs well in promoting wound healing and tissue regeneration (7). As such, we aim to elucidate the effect of the chitosan-assisted combination of laparoscope and hysteroscope on the levels of IFN-γ and ICAM-1 in the treatment of infertility caused by obstruction of fallopian tubes.

Materials and Methods

General data

A total of 100 patients with obstruction of fallopian tubes-caused infertility who visited Chongqing Jiangbei Hospital of Traditional Chinese Medicine between January 2019 and August 2021 were recruited into this study and divided into two groups as per the alternative method.

Criteria for inclusion: 1) Patients conforming to the related criteria for diagnosis and treatment according to the Obstetrics and Gynecology (8), including one of the following criteria: (i) Patient who had normal sexual life with no contraception or pregnancy, and whose husband’s reproductive function was normal; (ii) Patient with occlusion of fallopian tubes in recent years, and the combination of hysteroscope and laparoscope is widely accepted by clinicians and patients due to the minimal invasion, rapid recovery and painlessness. However, the operation...
sion at the proximal end of fallopian tube indicated by ute-
rotubography; (iii) Patient with occlusion at the proximal 
end of fallopian tube indicated by laparoscopic hydrotuba-
tion; 2) Patient who accepted the combination of laparos-
cope and hysteroscope operation and with no contraindica-
tion; 3) Patient who signed the written informed consents 
after they were informed of the protocols of this study.

Criteria for exclusion: 1) Patient with infertility due to 
the dysfunction in some organs; 2) Patient with cancer like 
cervical cancer, endometrium cancer and ovarian cancer; 
3) Patient who was allergic to the drugs used in this study. 
In Group A, there were 50 patients, aged between 25 and 
39 years old, with an average age of (31.27±2.58) years 
old; the duration of infertility ranged from 1 to 8 years, 
with an average of (3.38±1.62) years; there were 15 pa-
tients with primary infertility and 35 with secondary in-
fertility. In Group B, there were 50 patients, aged between 
24 and 38 years old, with an average age of (30.89±2.62) 
years old; the duration of infertility ranged from 1 to 7 
years, with an average of (3.40±1.58) years; there were 
17 patients with primary infertility and 33 with secondary 
infertility. Comparison of the general data between two 
groups showed no significant difference (P > 0.05), sug-
gest that the data were comparable. This study confor-
m to the requirement of the Declaration of Helsinki of 
the World Medical Association.

Methods

Patients in two groups underwent the combination of 
laparoscopic and hysteroscopic operation in the following 
steps: Operation was chosen within 3 to 7 days after mens-
tration; patients were required to stay in lithotomy posi-
tion for general anesthesia; Trocar was placed through the 
umbilical cord puncture to establish pneumoperitoneum 
(CO$_2$: 12mmHg) at the incision in the length of 5 mm at 
1.3 cm to the umbilical cord, 1.0 cm and 0.5 cm to the 
left lower abdomen. After the cervix uteri were dilated, 
a hysteroscope was inserted; thereafter, the fallopian tube 
was exposed by separating the pelvic adhesion to examine 
whether the fallopian tube was blocked by injecting the 
methylene blue. Under the guidance of a laparoscope, 
the catheter was delivered to the blocked site through the 
uterine cavity, where the syringe was pulled and pushed 
until the resistance disappeared, and then the fallopian 
tube recanalization was performed. Thereafter, methylene 
blue was injected and the appearance of blue liquid at the 
umbrella end indicated that the fallopian tube was unob-
structed. After treatment, the pelvic cavity was rinsed with 
normal saline and antibiotics were given in case of infec-
tion. Patients were advised to avoid any sexual intercourse 
within 1 month after treatment.

Patients in the control group underwent regular treat-
ment: Nutrition supplementation, fasting prior to the ven-
tilation for the gastrointestinal tract and administration of 
antibiotics according to the condition of the patient. For 
patients in the observation group, 3 mL of chitosan gel for 
medical use was smeared on the peritoneum of the pelvic 
and abdominal cavity and fallopian tube, followed by the 
closure of the abdomen.

Indicators for observation

The efficacy of patients in two groups was evaluated 
according to Obstetrics and Gynecology in the following 
criteria: Excellent for patients with the restoration of 
patency of oviduct and pregnancy within 6 months after 
treatment; effective for patients with the significant ame-
lioration of the stenosis in oviduct after treatment; failure 
for patients with no amelioration of the stenosis in oviduct 
after treatment. Total effectiveness rate = Rate of excellent 
+ Rate of effective.

Besides, 5 mL fasting venous blood was collected in the 
morning before treatment and 7 days after treatment, and, 
from the blood sample, the supernatant was obtained after 
the sample was centrifuged at 1000 rpm for 10 min. Later, 
the supernatant was prepared from the determination of 
inflammatory cytokines [Interferon γ (IFN-γ), intercellu-
lar adhesion molecule 1 (ICAM-1), interleukin 6 (IL-6)] 
and adhesion-related factors [laminin (LN), transforming 
growth factor β1 (TGF-β1) and fibronectin (FN)] via en-
zyme-linked immunosorbent assay (ELISA). Pelvic floor 
adhesion was also evaluated for all patients according to 
the Nair Classification Criteria: Grade I for a patient with 
only one adhesive band; Grade II for two adhesive bands; 
Grade III for a patient with bands more than 2 but with no 
adhesion of organ to the abdominal wall; Grade IV for a 
patient with bands more than 2 and with the adhesion of 
organ to the abdominal wall.

Statistical methods

SPSS 23.0 software was used to process and analyze 
the data. Measurement data were expressed in form of 
mean ± standard deviation (SD). Differences between the 
two groups were validated by the independent sample 
t-test. Enumeration data were expressed in form of a ratio, 
and the difference was validated by the chi-square test. P 
< 0.05 suggested that the difference had statistical signi-
nificance.

Results

Patients in Group B had a higher total effective rate 
as compared to those in Group A (92.00% vs. 76.00%), 
and the difference had statistical significance (P < 0.05; 
Table 1). Prior to the treatment, levels of IFN-γ, ICAM-
1 and IL-6 in patients of two groups had no significant 
difference (P > 0.05); after treatment, levels of indicators 
above experienced more evident decreases in Group B 
in comparison with Group A (P < 0.01; Table 2). Before 
treatment, levels of LN, FN and TGF-β1 of patients in two

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Excellent</th>
<th>Effective</th>
<th>Failed</th>
<th>Total effective rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>50</td>
<td>17 (34.00)</td>
<td>16 (32.00)</td>
<td>12 (24.00)</td>
<td>38 (76.00)</td>
</tr>
<tr>
<td>B</td>
<td>50</td>
<td>20 (40.00)</td>
<td>26 (52.00)</td>
<td>4 (8.00)</td>
<td>46 (92.00)</td>
</tr>
</tbody>
</table>

$\chi^2 = 4.762$  
P = 0.029
groups had no significant difference \( (P > 0.05) \); after treatment, patients in Group B had lower levels of LN, FN and TGF-β1 as compared to those in Group A \( (P < 0.01; \) Table 3). For pelvic adhesion, the incidence rate of patients in Group B was much lower than that in Group A \( (4.00\% \text{ vs. } 16.00\%; P < 0.05; \) Table 4).

### Discussion

Fallopian tube obstruction, as one of the major factors contributing to female infertility, can induce the hydrosalpinx and stenosis of the cavity to trigger the dysfunction in sperm transport, eventually leading to infertility. As the technique of endoscopes continues to improve, hysteroscope and laparoscope have been widely applied in the treatment of gynecological diseases by visualizing the site of the lesion and condition of the patient as well as the advantages, like slight trauma and good prognosis; besides, a combination of hysteroscope and laparoscope can further increase the effectiveness of surgery and ameliorate the clinical symptoms \( (9-10) \). However, surgery can only dredge the obstructed fallopian tube and restore the normal anatomic structure but fail to deal with the inflammation-induced pathological injury and maintain the long-term unblocked status of the fallopian tube, so medication in combination with surgery is quite meaningful for improving the efficacy and reducing the level of inflammatory factors. Results of this study demonstrated that as compared to Group A, patients in Group B had a higher total effective rate but a lower incidence rate of pelvic adhesion, suggesting that chitosan in combination with combined laparoscope and hysteroscope did increase the effective rate of treatment, increase the openness of fallopian tube and prevent the pelvic adhesion, which, according to our analysis, may relate to the good biological compatibility and degradability of chitosan that is conducive to the postoperative prophylaxis of adhesion.

Existing studies \( (11-12) \) have shown that surgical treatment can induce the injury, bleeding or stimuli of serosa, thereby inducing the hyperinflammatory responses in the serum of patients with fallopian tube obstruction. Local adhesion, as the inflammatory responses secondary to the fibroplasia, is somehow related to the level of inflammatory factors. Cell adhesion molecules can mediate allergic reactions, inflammation and thrombosis, where ICAM-1, as a key molecule, can recognize the specific receptor on the surface of cells to induce the adhesion, thereby being involved in the immune regulation and inflammation \( (13-14) \). IFN-γ, secreted by the nature of killing cells and T lymphocytes, can assist immune regulation and resist viral infection, showing a correlation with the severity of inflammation and injury to fallopian tubes \( (15) \). Zhao M Z et al. \( (17) \) predicted the pregnancy of patients with fallopian tube obstruction after the combined laparoscopic and hysteroscopic treatment by the levels of IFN-γ and ICAM-1 in serum and found that increased levels of IFN-γ and ICAM-1 are major risk factors inducing the postoperative infertility of patients. IL-6, as a kind of bioactive glycoprotein, plays a role in local or general anti-infection, and a high level of IL-6 can induce fibroplasia, thereby aggravating the injury to the fallopian tube.
and local pelvic adhesion; moreover, IL-6 can promote the formation of inflammatory scar, which could also contribute to the local adhesion and obstruction of the fallopian tube, eventually leading to infertility. Results of this study showed that after treatment, patients in Group B had lower levels of IFN-γ, ICAM-1, IL-6, LN, FN and TGF-β1 when compared to Group A, revealing that for fallopian tube obstruction, chitosan in combination with combined laparoscopic and hysteroscopic treatment can reduce the levels of IFN-γ and ICAM-1 and improve the levels of adhesion-related factors. Jiang et al. (18) evaluated the efficacy and safety of chitosan in preventing postoperative intestinal adhesion in 40 cases, and the results showed that chitosan can inhibit the levels of IL-1, TNF-α and TGF-β, thereby reducing the incidence of intestinal adhesion, which coincided with our findings. This is possible because the gel of chitosan can act as the lubricating factor and biological barrier that can prevent adhesion, and chitosan can promote the growth of epithelial cells but suppress the fibrotic cells selectively, thereby advancing the repairing of serosal cells.

In conclusion, chitosan in combination with combined laparoscopic and hysteroscopic treatment performs well in the treatment of fallopian tube obstruction by reducing the levels of inflammatory factors (IFN-γ and ICAM-1), improving the expression of adhesion-related factors and minimizing the incidence of pelvic adhesion.

References


