

## Original Article

# Distal fallopian tube recanalization using ozone treatment: a clinical study in two hundred tubal obstruction Chinese patients

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Received December 8, 2014; Accepted February 6, 2015; Epub February 15, 2015; Published February 28, 2015

**Abstract:** A major cause of female infertility is fallopian tube obstruction and traditional conservative and interventional treatments have been largely unsuccessful, especially in patients with distal tubal obstruction. The objective of the current study was to compare the curative outcome of ozone (treatment group) and conventional interventional treatment (comparison group) through comparing the different effects in the infertility cases caused by fallopian tube obstruction, with the purpose to provide future reference for better treatment regimen for tubal obstruction. 400 infertile cases caused by tubal obstruction admitted in the Second Affiliated Hospital of Shaanxi University of Chinese Medicine from August 2006 to January 2012 were enrolled in this study and received either ozone or conventional interventional treatment. No difference was observed between post-operative proximal tube recanalization rates in the two groups; however, post-operative distal tube recanalization rate and recanalization rate after 6 months were significantly higher in the treatment group. Importantly, the adhesion and conception rates were significantly lower and higher, respectively, in the treatment group compared to the comparison group after six months. Hence, ozone therapy can potentially become a viable treatment modality for far-end tubal obstruction patients.

**Keywords:** Tubal obstruction, ozone, infertility, distal tube, recanalization, adhesion, conception, pregnancy

## Introduction

It has been estimated that 8-10% couples are infertile globally, which in turn affects 60-168 million people worldwide [1-4]. This represents a growing socio-economic concern [5, 6]. Fallopian tube obstruction is the single major cause of female infertility, contributing to approximately 25-35% of the cases [7-11].

Even though The Practice Committee of the American Society of Reproductive Medicine (ASRM) laid down formal recommendations for using tubal cannulation for proximal tubal obstruction, there was no formal recommendation for treatment of distal tubal obstruction [11]. The fact of the matter is tubal surgery is still not the first line of treatment due to lack of convincing evidence of its success [12]; the aforementioned is true for both major invasive surgery [13] and microsurgery [14]. Despite recent innovations in assisted pregnancy and surgical tools, the lack of a convincing manage-

ment strategy combined with conflicting management strategies distorts the true pregnancy outcome rates [15]. This necessitates development of rationale strategies for treating tubal obstruction, especially distal tubal obstruction.

## Patients & methods

### Ethics

The current study was performed in accordance with the principles set out in the Declaration of Helsinki and was approved by the Institutional Review Board and Ethics Committee at the Shaanxi University of Chinese Medicine, Shaanxi, China. All patients were required to sign an informed consent document before being enrolled in the current study.

### Patients

Between August 2006 and January 2012, 400 female patients were chosen from 2600 female

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**Table 1.** Outcome measures in the tow (treatment and control) intervention groups

	Recanalization rate after operation		Recanalization rate after 6 months	Re-adhesion rate	Pregnancy rate after 12 months
	Proximal segment	Distal segment			
Treatment group	85% (170/200)		93% (186/200)	5% (10/200)	59% (108/200)
	94%	56%			
Control group	81% (162/200)		79% (158/200)	21% (42/200)	43% (86/200)
	93%	45%			

patients admitted to the Second Affiliated Hospital of Shaanxi University of Chinese Medicine for recanalization surgery. The inclusion criteria were angiography-mediated pre-operative diagnosis of tubal obstruction and concurrent exclusion of other potential causes of infertility. Infertility definition was approved as per global recommendations [11]. The 400 tubal obstruction patients were randomly divided, 200 each, into the treatment group (receiving ozone treatment) and control group (receiving standard interventional therapy).

### Methods

**Intervention-treatment group:** The tubal recanalization apparatus (Cook Company, U.S.) was used to perform surgery 3 to 7 days after menstrual clean. The patients were sublingually administered with atropine (1 mg) before surgery. Patients were placed in the lithotomy position, vulva was regularly disinfected with povidone-iodine, and the drape was placed into a vaginal speculum via the vagina. After exposure of the cervix, the cervix was disinfected again, the upper lip of the cervix was clamped with cervical clamps, and 76% meglumine diatrizoate or ominipaque was injected by inserting the uterine catheter via the cervix to conduct angiography so as to determine the site and degree of obstruction. 9F catheter, 5.5F catheter and 3F catheter were loaded into the uterine cavity in sequence, and the 3F catheter was inserted at the opening of the oviduct on the obstruction side. About 5-10 ml of medical ozone was slowly injected via the 3F catheter under pressure to observe whether there was gas shadow in the pelvic cavity or whether the patient had any discomfort. The fallopian tube recanalization was indicated when the operator felt no resistance during injection, and then contrast agent was injected to confirm the non-obstruction of the oviduct. Ozone was injected every alternative day in treatment group for 1-2 times after surgery, and ozone was injected 3-7 days after menstrual clean in the next menstru-

ation for 1-2 times, with no concurrent anti-inflammatory treatment.

**Intervention-control group:** After the intervention treatment as for the treatment group, 20 ml of saline solution containing 5 mg of dexamethasone, 4,000 units of chymotrypsin and 80,000 units of gentamicin were injected into the fallopian tube.

### Follow-up

All enrolled patients were scheduled for an outpatient review 6 months after intervention. This was subsequently followed-up by telephone calls after another 6 months to determine conception rate.

### Results

All patients in the control and treatment groups had varying degrees of vaginal bleeding, abdominal distension, and abdominal pain. A few number of patients in the treatment group also had subcostal pain. No serious adverse reaction or allergic reactions were reported in any of the patients in the treatment group. In the treatment group, a small amount of subphrenic free gas was found in combination with X-ray examination.

As shown in **Table 1**, proximal tubal recanalization rate (94%) of the treatment group and the control group (93%) had no significant post-operative difference ( $P > 0.05$ ). However, contrary to the proximal recanalization rate, post-operative distal recanalization rate of the treatment group (56%) was significantly higher than that in the control group (45%) ( $P < 0.01$ ). The overall recanalization rate was significantly higher in the treatment group (93%) as compared to the control group (79%) 6-months after intervention ( $P < 0.01$ ).

The re-adhesion rate in the treatment group was significantly lower than the control group ( $P < 0.01$ ) (**Table 1**). Importantly, the pregnancy

rate after 12 months of intervention was significantly higher in the treatment group (59%) compared to the control group (43%) ( $P < 0.05$ ).

## Discussion

Tubal obstruction has varied pathogenesis, all contributing to non-specific inflammation. However, chronic pelvic inflammatory disease (PID) or chronic salpingitis contributes to 50% of all tubal obstruction cases [11]. Effective treatment of the primary disease is also often complicated by post-operative adhesions [11]. Traditional tubal recanalization has been widely used clinically for many years, but its efficacy in patients with distal tubal obstruction is unsatisfactory. Hence, more robust regimens are required for interventional physicians and obstetricians to ameliorate tubal obstruction in general and distal tubal obstruction in particular.

Ozone has high oxidative potential and ozone therapy can stimulate production of immunoglobulins in the blood, thus making it a potent agent to treat microbe-mediated gynecological inflammation. In addition, ozone treatment improves the rheological properties and oxygen transportation mechanism of the blood, in turn destroying contact points of virus with body cells. The advantage using ozone is that it does not have adverse effects commonly associated with other antimicrobials and microbes cannot develop resistance to ozone. Moreover, ozone treatment does not change the pH of the female reproductive system thus preserving the beneficial vaginal flora [16].

Ozone has been used in the clinical treatment of gynecological inflammation and has shown significant efficacy in resolution of inflammation. Catheter-mediated pressure injection of high concentrations of ozone can physically break down adhesions, effectively break down inflammatory tissue and inhibit inflammation, and can quickly promote the healing of wounds resulting from separating the adhesions. In the current study, the re-adhesion rate of 5% observed in the treatment group is significantly lower than obtained in other studies [16].

In summary, our results are highly encouraging and hold promise for treating distal tubal obstruction in infertile females. The large number of patients involved in the current study

also makes the conclusions more robust. However, random clinical trials and longer follow-up are required to realize the true potential of ozone treatment intervention in curing tubal obstruction.

## Disclosure of conflict of interest

None.

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