

Ozone Treatment for Chronic Anal Fistula: It Is Not Promising

Alaattin Ozturk¹ · Talha Atalay¹ · Gokhan Cipe¹ · Nurettin Luleci²

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Abstract The aim of this study is to assess the effect of ozone gas in the treatment of anorectal fistulae. The tip of a 20 G intravenous cannula was inserted from the fistula orifice. Medical ozone was introduced into the fistula. A total of 10 sessions of ozone gas insufflation was performed on alternate days. Treatment was considered to be successful if fistula discharge ceased and the outer fistula orifice closed; however, if discharge was continued or outer fistula orifice was open, the treatment considered to be failed. A total of 12 adult patients were included in the study. The fistula was closed in three patients (25 %), in nine patients (75 %) without closure. In one patient who had fistula closure, the fistula recurred after 2 months. Patients did not express any discomfort during ozone insufflation. There were no side effects or complications due to ozone insufflation. The success rate of ozone insufflation in anorectal fistulae closure is low.

Keywords Anorectal fistula · Medical ozone · Ozonide · Adult · Anal discharge

Introduction

Anorectal fistula is an enterocutaneous fistula that develops after spontaneous or surgical drainage of an anorectal abscess.

✉ Alaattin Ozturk
aloz1969@yahoo.com

¹ Department of General Surgery, Fatih University Medical Faculty, Yalı Mh. Sahilyolu Sk No: 16 Maltepe, 34844 Istanbul, Turkey

² Department of Algology, Fatih University Medical Faculty, Yalı Mh. Sahilyolu Sk No: 16 Maltepe, 34844 Istanbul, Turkey

It causes discharge, moisture, and a recurrent abscess in the perianal region. Spontaneous recovery cannot be expected. The main treatment for anorectal fistula is surgery. The aim of treatment is to eliminate the fistula, prevent recurrence, and maintain anal continence. Postoperative recurrence and development of incontinence are serious problems for these patients. Hence, various treatments are being investigated for anorectal fistula.

Ozone is a natural gas composed of three oxygen atoms. It is a powerful disinfectant, inactivating a large number of pathogenic bacteria. It also offers recovery-enhancing effects by stimulating cell proliferation [1, 2]. It has been demonstrated to be an effective, practical antibacterial agent [3]. Medical ozone is composed of 5 % ozone and 95 % oxygen. When dissolved in circulating blood, it has antioxidant effects on many organs and tissues through oxygen radicals and lipid oxidation products. The mechanism of action of ozone in the body has been described in detail in the literature [2, 4].

Ozone has been used to treat various diseases, including infectious, ischemic, and neurodegenerative diseases; cancers; autoimmune diseases; dental diseases; and degenerative lumbar diseases [2]. For treating those various entities, ozone is supplied to the body in various ways: intravenously, intramuscularly, subcutaneously, intraperitoneally, intrapleurally, intraarticularly, intralesionally, nasally, urethrally, and rectally [1, 2, 4].

Ozone gas has been used to treat some chronic inflammatory diseases similar to anorectal fistula disease because of its healing effects [1, 2]. It has not, however, been used to treat anorectal fistulas. In this prospective, single-arm study, we aimed to assess the healing rate of chronic anal fistulas in adult patients after ozone gas insufflation to the fistula tract.

Materials and Methods

This single-arm study was performed prospectively. Anorectal fistula was detected in 36 patients with anal discharge who were admitted between June 2011 and January 2012. Surgery or ozone gas insufflation was offered to the patients as options for treating the fistula. The advantages and disadvantages of surgical treatment and ozone insufflation were explained. Written informed consent was obtained from all patients who selected ozone treatment. The institutional ethics committee approved the study.

Patients without active infection who had one fistula orifice and who preferred ozone insufflation were included in the study. Patients with infected discharge, concomitant anal disease, or multiple external orifices were excluded from the study. All patients completed the planned treatment. The effect of the ozone treatment applied to the anorectal fistula and its side effects were evaluated at the end of the study.

Patients were placed in the prone position for ozone insufflation. No sedative, anesthetic, or analgesic drugs were used during the insufflation process. The outer orifice of the anorectal fistula was identified, and the tip of a 20-gauge intravenous cannula was inserted 2–3 mm from the fistula orifice. Medical ozone obtained from an ozone production device (Humazon® Promedic; Humares GmbH, Bruchsal, Germany) was pulled into the injector, and the injector was introduced into the fistula. Ozone concentrations were adjusted to be within the range of 10–40 µg/ml according to the amount of discharge from the fistula. Higher concentrations of ozone were insufflated in patients with greater discharge. The volume of ozone was adjusted to within the range of 60–180 ml according to the patient's sensation of the gas in the rectum. The cannula was removed after gas insufflation. There was no need for any dressing after the insufflation.

Ten sessions of ozone gas insufflation were planned on alternate days for each patient. Five or more sessions were added for patients who showed significantly reduced amounts of discharge. Treatment was considered effective if the fistula discharge ceased and the outer fistula orifice closed at the end of the treatment period. If the discharge continued or the outer fistula orifice remained open, however, the treatment was considered a failure. None of the patients was given antibiotics.

A 1-year follow-up was planned, at which time patients were evaluated for the presence of a discharge. The success rate was expressed as a percentage. A *t* test was used when comparing the number of sessions for healing and non-healing patients. A value of $p < 0.01$ was regarded as indicating significance.

Results

Between June 2011 and January 2012, a total of 36 patients presented with anal discharge. In all, 12 of them who accepted

ozone treatment were enrolled in this study. We excluded patients who do not accept ozone treatment or who had concomitant anal disease. All of the patients presented with a chronic anal fistula with discharge.

All 12 patients completed the study. The study group consisted of 1 woman and 11 men (mean age 38 years, range 28–49 years). One patient had previously undergone surgery for the fistula, but it had recurred. The other 11 patients had not undergone any previous treatment.

Overall, at the end of the ozone treatment, the fistula had closed in three patients (25 %). Among them, ozone was insufflated during four sessions in one patient and during six sessions in two patients. Nine patients (75 %) had no closure. Among those patients, ozone was insufflated in three patients during 15 sessions and in six patients during 10 sessions. The patients in whom fistula closure was observed underwent fewer ozone insufflation sessions (Table 1).

Patients did not express any discomfort during the insufflation. There were no side effects or complications due to the ozone treatments in any of the patients.

In one patient who experienced fistula closure, the fistula recurred 2 months later. Physical examination revealed that the patient had a recurrent fistula, and ozone insufflation was considered to have failed. There was no recurrence during the 1-year follow-up in one patient or during the 2-year follow-up in the third patient. Thus, the overall success rate (closure of the fistula orifice because of ozone insufflation) was 25 % in this study.

Discussion

According to the results of our study, fistula closure was achieved in 3 of 12 patients. Cessation of discharge and a closed fistula orifice were considered signs of closure in these patients. The fistula relapsed in one patient. No side effects occurred in any of the patients. Ozone insufflation was well tolerated by the patients.

The easy application of ozone insufflation and easy assessment of the treatment are the advantages of this study. The small number of patients is the study's major limitation.

Ozone is a known treatment for anal abscesses, ulcerative colitis, and Crohn's disease [2]. It has also been studied as a treatment for enterocutaneous fistula [1]. Moreover, one study found that ozone decreased the severity and mortality of experimental acute necrotizing pancreatitis in rats [5]. Another showed that intraperitoneal ozone insufflation increased healing of colonic anastomoses [6]. When ozone was used as an adjuvant treatment in experimental distal colitis, improvement was reported [7]. We hypothesized that ozone could be useful for treating anorectal fistula disease because it had been observed to promote tissue healing and reduce inflammation during other fistula treatments. Therefore, to

Table 1 The results of the patients

Age/gender	Concentration of ozone ($\mu\text{g/ml}$)	Volume of ozone (ml)	Number of session	Result	Follow-up
32/M	10–40	180	6	Closed	2 years
38/M	10–20	80	4	Closed	1 year
26/M	10–20	60	6	Closed ^a	2 months
41/M	10–20	60	10	No closure	–
46/M	10–40	60	10	No closure	–
41/M	10–20	120	10	No closure	–
38/F	10–20	120	10	No closure	–
35/M	10–20	180	15	No closure	–
43/M	10–20	120	15	No closure	–
49/M	10–20	60	15	No closure	–
39/M	10–40	120	10	No closure	–
28/M	10–20	120	10	No closure	–

^a The fistula relapsed 2 months later

identify a possible new treatment for anorectal fistula that would avoid surgical intervention and incontinence, we designed a study to investigate the effects of ozone treatment in patients with anorectal fistula.

Adjusting and then achieving the desired dose could be difficult during rectal ozone insufflation as the colonic content and thick mucus layer might reduce the efficiency of the ozone. Also, with ozone insufflation through the rectum, it could be difficult to calibrate the dose to achieve the desired amount. An average ozone concentration of 30 $\mu\text{g/ml}$ was used for rectal insufflation in a previous study. It is recommended that rectal ozone insufflation should not be performed rapidly, and the initial dose should be 3–5 $\mu\text{g/ml}$, which may be slowly increased if the patient tolerates it well. Otherwise, the ozone may lead to painful abdominal cramps [2].

We started with an ozone concentration of 10 $\mu\text{g/ml}$ and increased it until it reached 40 $\mu\text{g/ml}$. We then increased the volume of the gas until the patient felt it in the rectum. We were able to reach a maximum of 180 ml. Ozone gas can be insufflated every day or on alternate days [2]. We preferred to insufflate on alternate days for the convenience of the patients in this study.

An average of 4.6 sessions was completed by patients with successful closure of the fistula, whereas an average of 11.6 sessions was completed by those with no closure. A *t* test was performed, and the number of sessions between the two groups was found to be statistically significant. Based on this result, fewer ozone sessions were sufficient for fistulas that had a possibility of closure.

In our opinion, ozone insufflation could be an alternative treatment in patients with an uncomplicated, uninfected, short fistula tract. We think that granulation tissue, which is resistant to recovery and covers the inner fistula, prohibits closure. Although 25 % resolution is not a high percentage, it could support the use of ozone therapy as a trial for aged patients or

patients with co-morbidities before attempting surgery, especially if there is a short-tract fistula.

Although the low success rate is disappointing, it may be increased with further research on the issue. Particularly in patients with a short-tract fistula, a higher success rate could be achieved with debridement of the granulation tissue. A shorter, straighter fistula tract might be advantageous for closure.

Ozone gas saturated by water or olive oil is called ozonide. Because the half-life of ozone in ozonide is longer than that of ozone gas alone [2], its activity in tissue lasts longer. The use of ozonide to ensure long-term ozone contact on the whole surface of the fistula tract might provide better results. In addition, performing perianal magnetic resonance imaging before and after insufflation would be helpful for showing objective improvement with ozone.

Based on the results of our study, the success rate of ozone insufflation to achieve anorectal fistula closure is low. There were no side effects of applying ozone to the anorectal fistula.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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