Original Article

Intraprostatic ozone therapy: A minimally invasive approach in benign prostatic hyperplasia

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Abstract

Introduction: Transurethral resection of prostate (TURP) remains the golden standard therapy since decades. There are various minimally invasive therapies (MITs) for the treatment of benign prostatic hyperplasia (BPH). Still, there is a need for therapy with lesser side effects and better outcome. We had studied the effect of intraprostatic ozone injection (IPOI) as an MIT for patients with BPH who have failed trial without catheter (TWOC).

Materials and Methods: Thirty elderly patients with BPH with a prostate size of 30 g or more were enrolled for the study. Forty milliliters of ozone at a concentration of 30 μg/dl was injected in prostate (20 ml in each lateral lobe) per rectally. Prostate volume (PV) by ultrasonography was assessed after catheter removal on the 7th day and after 1 month.

Observations and Results: Totally thirty patients (mean age - 67.8 years) with mean prostatic volume (MPV) of 46.10cc received IPOI. MPV came as 44.96cc on the 7th day of postozone therapy ($P = 0.008$). Successful voiders showed a significant reduction in PV (mean = 13.12cc) as compared to unsuccessful voiders (mean = 2.61cc) after 1 month.

Conclusion: Intraprostatic ozone injection helps to reduce the PV to some extent and can be helpful in patients who have failed TWOC even on alpha blockers and are unfit for TURP. Larger studies are required to assess the efficacy and long-term results of this technique.

Key Words: Benign prostatic hyperplasia, intraprostatic ozone therapy, minimally invasive

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INTRODUCTION

Benign prostatic hyperplasia (BPH) contributes a lot in lower urinary symptoms in aging men. Transurethral resection of prostate (TURP) remains the golden standard therapy since decades. Pharmacotherapy recommended for BPH include α-adrenergic blockers, 5α-reductase inhibitors, aromatase inhibitors, and numerous plant extracts had largely replaced the surgical treatment but always not successful in every patient of BPH.[1] Associated comorbid conditions and morbidity of the surgical procedure sometimes require an alternative nonsurgical minimally invasive treatment to reduce the prostate size.

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Ozone gas is used in the treatment of certain medical conditions utilizing its anti-inflammatory properties. It was used in protruded disc for dissecation as a treatment of prolapsed intervertebral disc cases. The effect of ozone motivated Vitoria[2] to use ozone in few patients with BPH for symptomatic improvement. This study was carried out on the basis of this hypothesis.

We had studied the said effect of ozone on prostate size reduction by intraprostatic ozone injection (IPOI). Patients were assessed for prostate size reduction and successful trial without catheter (TWOC) after IPOI.

MATERIALS AND METHODS

The prospective study was conducted in the department of surgery in a tertiary care hospital from January 2013 to January 2015 after obtaining approval from the college's Ethics Committee.

Inclusion and exclusion criteria

All the patients with BPH in whom TWOC after alpha blocker had failed were enrolled for the study. All patients of prostate size of 30 g or more were included in the study with their willingness for ozone therapy after explaining the standard treatment of BPH, i.e., TURP. Any patient with concomitant bladder pathology, such as neurogenic bladder, and patients with abnormal digital rectal examination or raised prostate-specific antigen were excluded from the study.

Material required

- Medical-graded ozone generator (Waterhouse Company) for ozone production
- One 23 Fr spinal needle
- One 50 ml disposable syringe.

Procedure

Patients with BPH in whom TWOC after alpha blocker had failed were admitted in ward after initial examination and investigation. These patients were explained the IPOI procedure as well as the standard treatment of BPH. Explained, informed written consent was taken from the patients after their willingness to IPOI. Procedure was done in the operation theater under proper aseptic precaution, and prophylactic antibiotics were given.

Patients were placed in Sim's position on the operating table, and preprocedure per rectal examination was done. In all the selected patients, 40 ml of ozone at a concentration of 30 μg/dl was injected at multiple sites (20 ml in each lateral lobe) through 23 Fr spinal needle. Patients were observed for 30 min after the procedure. Catheter was removed after 7 days. Patients were assessed for prostate volume (PV) by transabdominal ultrasonography (USG). Prostate size assessment was done by per abdominal USG at 7th day and after 1 month.

RESULTS

Totally thirty patients with a mean age of 67.8 years were included in the study. Eight patients (26.6%) had some medical comorbid conditions, namely, chronic obstructive pulmonary disease, ischemic heart disease, hypertension, diabetes mellitus, and thrombocytopenia. All patients had uneventful postozone therapy course with mild pain at injection site ($n = 5$) and perianal rash in two patients which subsided within 24 h.

USG was done in all patients before ozone treatment. Prostatic volumes of all patients were assessed. It ranged from 32 to 94cc (mean - 46.10cc).

USG was done in all patients on the 7th day after ozone therapy. Fourteen patients (46.7%) showed the reduction in the volume of prostate. Sixteen patients (53.3%) showed no change in the volume of prostate [Table 1]. Mean prostatic volume (MPV) came as 44.96cc on the 7th day of postozone therapy ($P = 0.008$).

All patients were reassessed by USG after 1 month for PV.

Totally 22 patients were turned up after 1 month for follow-up, of which 17 patients (56.7%) showed further reduction in prostate size. MPV was reduced from 44.96 to 42.7cc after 1 month. Four patients did not show any change in the volume of prostate. One patient showed an increase in the size of prostate. MPV after 1 month came out to be 42.7cc.

Successful voiders (void with uroflow rate of at least 10 ml/min) showed a significant reduction in PV (mean = 13.12cc) as compared to unsuccessful voiders (mean = 2.61cc) [Table 2]. Five patients of unsuccessful voiders group showed further improvement of their symptoms.

Table 1: Effect of ozone on prostate size

Effect of ozone on PV	Number of patients on the 7th day (%)	Number of patients on 1 month (%)
PV reduced	14 (46.7)	17 (56.7)
No effect	16 (53.3)	4 (13.3)
Increased PV	0	1 (3.3)

PV: Prostate volume

Table 2: Prostate volume reduction between successful voiders and unsuccessful voiders

Improvement	Cases voided	Cases not voided
Mean PV reduction	13.12	2.61
SD	2.4	4.6
Number of cases	5	16

SD: Standard deviation, PV: Prostate volume

DISCUSSION

The precise molecular etiology of this prostatic hyperplastic process is uncertain. The observed increase in cell number may be due to epithelial and stromal proliferation or due to impaired programed cell death leading to cellular accumulation. It might be induced by local growth factor or growth factor receptor abnormalities. An additional source of growth factors in human BPH tissue may be the inflammatory cell infiltrates seen in many men with BPH.[1]

Ozone (O_3), an inorganic gas discovered in the mid-19th century, is a molecule consisting of three atoms of oxygen (O_3). Ozone has many industrial and consumer applications related to oxidation.[3] Ozone has a capacity to oxidize organic compounds, and researchers believe that it has many therapeutic effects such as ozone therapy. It is the use of ozone gas to treat certain medical conditions and most commonly practiced in Europe.[4]

Ozone exerts its power through its metabolites: The peroxides, promoting the formation of prostaglandins of both pro- and anti-inflammatory types. These prostaglandins are mediators in the transmission of the message which trophic hormones such as luteinizing hormone, thyroid-stimulating hormone, and adrenocorticotropic hormone produce on the effecter cells. In turn probably these prostaglandins activate the formation of cyclic adenosine monophasphate, which stimulate effecter cell function.

This effect of ozone motivated Vitoria[2] to use ozone in few patients with BPH for symptomatic improvement. This study was carried out on the basis of this hypothesis.

In our study, intraprostatic injection of ozone gas in patients with BPH had shown some beneficial effects. Nearly 46.7% of the patients had shown the reduction in prostatic volume which was assessed by USG. Only five patients relieved from retention but showed a significant reduction in prostatic volume after 1 week (mean = 13.2cc).

There was no complication after the ozone therapy. Patients with medical comorbid conditions also tolerated the procedure very well. Prostatic volume further decreased after 1 month follow-up (MPV - 42.73cc) with improvement in symptoms in five patients.

Vitoria also assessed the effect of intraprostatic ozone in nine patients with features of BPH. He had injected ozone through perineal route in multiple sessions and assessed the improvement of symptoms. Six patients showed favorable outcome with improvement of symptoms.

A small number of patients had shown improvement in our study with single session of ozone injection as compared to Vitoria's study who had given ozone in multiple sessions.

Ozone has shown excellent health benefits in dental caries.[5] When ozone gas was applied topically to infected wounds, it not only remedied infection, but also had hemodynamic and anti-inflammatory properties.[4] Ozone therapy is useful in the treatments of lumber disc herniation[6] and osteoarthritis of knee joints[7] owing to its anti-inflammatory properties.

Ozone injections (intra-articular, peri-articular, or percutaneous) are considered as good treatment with a high success rate and a resolution of joint pain, with good functional recovery. It has shown to be with little risk of complications, easy execution, repeatability, and good outcome.[8] Intra-articular injections of ozone relieved pain, stiffness, and physical disability better than intra-articular injection of methylprednisolone[7] and internal derangement of the temporomandibular joint.[9]

Combination therapy with the use of ozone therapy and tamsulosin can be successfully and safely used in the treatment of patients with chronic cystitis.[10]

All these studies had shown the therapeutic use of ozone in various fields including urology.

There is sufficient evidence that ozone can be used in patients with BPH. This procedure requires further study in a large number of patients, may be in multiple doses.

CONCLUSION

Intraprostatic ozone injection helps to reduce the PV to some extent and can be helpful in some patients who have failed TWOC even on alpha blockers and are unfit for TURP. This is a minimally invasive procedure which can be performed easily without any major complication or problem. This procedure can be useful in some patients where standard treatment option cannot be contemplated. Larger studies are required to assess the efficacy and long-term results of this technique.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Roehrborn CG, McConnell JD. Benign prostate hyperplasia:etiology, pathophysiology,epidemiology and natural history. Wein AJ, editor. Campbell Walsh Urology. 9th ed., Ch. 86. Philadelphia: Saunders, Elsevier; 2007.

2. Vitoria JF. Benign prostatic hypertrophy (BPH) treated with ozone therapy. Int J Ozone Ther 2009;8:75-9.
3. Rubin MB. The history of ozone. The Schönbein period, 1839-1868. Bull Hist Chem 2001;26:40-56.
4. Elvis AM, Ekta JS. Ozone therapy: A clinical review. J Nat Sci Biol Med 2011;2:66-70.
5. Holmes J. Clinical reversal of root caries using ozone, double-blind, randomised, controlled 18-month trial. Gerodontology 2003;20:106-14.
6. Andreula CF, Simonetti L, De Santis F, Agati R, Ricci R, Leonardi M. Minimally invasive oxygen-ozone therapy for lumbar disk herniation. AJNR Am J Neuroradiol 2003;24:996-1000.
7. Mishra SK, Pramanik R, Das P, Das PP, Palit A K, Roy J, *et al*. Role of intra-articular ozone in osteo-arthritis of knee for functional and symptomatic improvement. IJPMR 2011;22:65-69.
8. Benvenuti P. Oxygen-ozone treatment of the knee, shoulder and hip – A personal experience. Riv Ital Ossigeno Ozonoterapia 2006;5:135-44.
9. Daif ET. Role of intra-articular ozone gas injection in the management of internal derangement of the temporomandibular joint. Oral Surg Oral Med Oral Pathol Oral Radiol 2012;113:e10-4.
10. Smeliakov VA, Borisov VV. Ozone therapy and tamsulosin in the treatment of cystitis. Urologiia 2013;1:38-40.